



# The Law of the Lab: Using Zerit to Inform Technology Transfer

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The Law of the Lab:  
Using Zerk to Inform Technology Transfer

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**ABSTRACT.** *The author takes a comprehensive look at the government's policy of technology transfer, the process by which government-funded inventions are transferred to the private sector for commercialization. Emphasis is placed on biomedical R&D and, in particular, on pharmaceutical drugs. The author describes how the Bayh-Dole Act of 1980 fundamentally altered the government's approach to tech transfer. He explains why the Act is viewed as a success, and presents the three most significant current debates over the policy's future. These debates, the author argues, can be informed by careful study of how tech transfer operates in practice. For this reason, the author then presents, in narrative form, the development of Zerit, an effective AIDS medication supported by government funding and then transferred to Bristol-Myers Squibb for commercialization. This narrative is then used by the author to inform the three current debates over tech transfer. The author finds that the Bayh-Dole Act is generally successful, but that the government should do more to ensure that taxpayers are maximizing the return on their investment. The author also finds that the government should take greater care to consider not only international trade, but also public health, national security and ethical responsibility, when deciding whether to exercise government rights to taxpayer-funded inventions.*

## Introduction

Technology transfer, the policy that regulates the transfer of government-funded inventions to the private sector for commercialization, plays a critical role in promoting economic growth, improving public health, and ensuring national security. Twenty years have passed since the Bayh-Dole Act of 1980 fundamentally altered the government's approach to this policy. The Act, which encouraged the use of exclusive licenses to stimulate private commercialization of government-funded inventions, is now widely heralded as a success. In the field of biomedical research, the number of FDA-approved medications has skyrocketed, and hundreds of small biotech firms are busy pushing potential medications through the product pipeline. But the Act is not without critics. Some label the policy an unnecessary corporate windfall; others argue that it is constricting the free and open exchange of information that is essential to scientific progress.

This article takes a comprehensive look at just how successful the Bayh-Dole regime of technology transfer has been in the field of biomedical research. Section I provides both an overview of tech transfer and a review

of its historical development. In Section II, the author examines why many believe Bayh-Dole is a success. Then, the three main debates that dominate discussion over the future of tech transfer are presented: whether exclusive licenses are in fact necessary to encourage commercialization, whether taxpayers are maximizing the return on their investment, and whether the policy might be unintentionally impeding scientific progress. The author argues that each of these debates suffers from a lack of information and could be informed by careful study of the development of particular drugs.

Section III consists of a narrative account of the development of Zerit, an effective AIDS medication supported by government funding and then transferred to Bristol-Myers (now Bristol-Myers Squibb) for commercialization. This narrative is then used, in Section IV, to inform the three current debates. The author finds that the development of Zerit largely confirms that the exclusive licenses encouraged by Bayh-Dole are having their desired impact. Nevertheless, Zerit also indicates that some tinkering in the policy may be in order. Specifically, Zerit reveals that taxpayers may not be maximizing the return on their investment, and that concerns that Bayh-Dole is restricting the open exchange of scientific data should be taken very seriously. Zerit also reveals that the government should take greater care to exercise its rights to government-funded inventions in accord with not only international trade, but also public health, national security and ethical responsibility. Finally, the author recommends making tech transfer more effective by distinguishing essential medicines like Zerit from other medicines, and then reserving for the government greater background rights in the former.

# **I.**

## **Technology Transfer: The Public Pursuit of Scientific Progress**

Technology transfer policy is as complex as the ever-changing research and development (R&D) that it regulates. This section of the article provides an overview of this complicated policy and describes how it evolved to its current state. As the focus of this article is pharmaceutical drug development, special attention is given to the biomedical R&D funded and coordinated by the National Institutes of Health (NIH). The section concludes with a discussion of five salient features of the policy's historical development.

### **I.A. Introduction to Technology Transfer**

In a sentence, technology transfer is the process by which government-funded inventions are transferred to the private sector for further development and commercialization.

Technological advance is often depicted as the product of enterprising individuals who, motivated by either professional prestige or financial success, discover the medicines and the machines that push society forward. It is a beautiful image, but it is also somewhat of an over-simplification. Technological advance is in fact the product of a complex array of incentives and actions. It is certainly driven, in part, by individuals seeking prestige, pursuing personal profit, or perhaps just scratching an inventive itch. It is also driven, in part, by luck. And it is also driven, in part, by the government.

There are a number of rationales supporting government support for technological and scientific progress. First, inventors motivated by financial profit need property rights – patents – to secure their potential inventions. To induce these inventors to work their magic, the government passes patent laws, secures

property rights, and guarantees enforcement of those rights. Second, government intervention is at times necessary to overcome market failure. Private industry, for example, may be discouraged from engaging in research that takes too long or is too risky (such as basic, foundational biological research). Such endeavors are not well suited to a corporation's purpose, namely, maximizing shareholder value. Alternatively, market failure may occur where maximum profit does not align with maximum human health and welfare. There is more profit, for example, in a pill taken once a day for the rest of a patient's life than there is in a vaccination that individuals need take only once.

The third reason why the government may decide to stimulate R&D is simply to speed things up. Patents may be enough to encourage private investors and inventors to discover pharmaceutical drugs. But, why wait for private investors and inventors to cure cancer or AIDS? Why not speed up the process by contributing public funds to the cause? Fourth, and finally, the government may wish to stimulate R&D because technological advance stimulates overall economic growth. The Internet is perhaps the most salient example of how a government-funded invention can drive economic growth. Similarly, pharmaceutical drugs stimulate economic growth by making workers more productive (fewer sick days and longer lives) and reducing the costs of procedures and hospitalization.

For these reasons, the government spends billions of dollars annually on R&D in biomedicine, defense and countless other fields. The NIH, the Department of Defense (DoD), the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA) and many other government agencies fulfill their mission at least in part by supporting technological advance. In 1995, federal funding accounted for approximately 36% of total national outlays for R&D, and 58% of outlays for basic research.<sup>1</sup>

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<sup>1</sup>Rebecca S. Eisenberg, *Technology Transfer in Government-Sponsored Research*, 82 Va. L. Rev. 1663, 1667 (1996).

The value of spending a portion of the federal budget on such R&D is, for the above-mentioned rationales, clear and uncontroversial. Evidence of this is the fact that both the Clinton and the Bush administrations backed significant increases in the NIH budget. At the same time, unclear and quite controversial is how to get the most mileage out of this government support. Who should receive this funding? What background rights should taxpayers retain in inventions? Some argue for leaving these inventions in the public domain. This enables future scientific progress to build off of past achievements. It also opens the door for multiple private entities to commercialize the product, ensuring an open, competitive market among suppliers. On the other hand, if an invention is left in the public domain, then it is possible that no company will risk investing in its commercialization. If this occurs, and the invention is left to languish on the floor of a government laboratory, then nobody benefits.

Determining the proper level of incentives that are necessary to ensure that government-funded inventions are commercialized has driven and continues to drive the development of tech transfer. The incentive typically comes in the form of property rights, either patents or licenses, to the invention. The nature of these property rights is the central focus of this paper. The fundamental goal of technology transfer policy is to strike a balance between the rights of private industry and the rights of the taxpayers in a way that maximizes public welfare.

### **I.B. Technology Transfer in Practice: Focus on Biomedical Technology**

Before turning to the historical development of tech transfer policy, it is worth taking a snapshot of how the policy works. Again, as the focus of this article is pharmaceutical drug development, special attention

is given to R&D coordinated by the NIH.

### I.B.1. A Giant Public-Private Partnership

The process of drug development might be viewed as one giant public-private partnership. In the words of Jeff Trewhitt, a spokesman for the Pharmaceutical Research and Manufacturers of America (PhRMA), “there has been an honorable division of labor.”<sup>2</sup> This division of labor generally works as follows: Taxpayers support foundational research into potential health care technologies in the preclinical phase (both in government laboratories and at universities), and then private industry supports further development. This further development typically involves clinical trials, the FDA approval process and commercialization. All phases of drug development are risky. PhRMA reports that of every 5,000 medicines that are tested, only 0.1% (5) emerge from the preclinical phase. Of these five medications, only 20% (1) survives clinical testing and the approval process. The federal government funds about 42% of all health care research. The private sector funds about 55%, and the remainder is funded by other government agencies and by nonprofit institutions, such as foundations.<sup>3</sup> Thus it may fairly be said that taxpayers play a significant and essential role in the drug development process, and the same may fairly be said of private industry. Indeed PhRMA reports that “the value of both public- and private-sector research to patients is priceless.”<sup>4</sup>

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<sup>2</sup> *Taxpayers Pay Twice for New Medicines* (visited July 24, 2001) <www.cnn.com>.

<sup>3</sup> It is estimated that nationwide total spending on health-related R&D in 1999 was \$45.5 billion: \$19.2 billion contributed by the government (42%), \$24.8 billion contributed by industry (55%), and the remainder contributed by private foundations and nonprofit organizations. These figures do not include the numerous tax breaks given to private industry conducting biomedical R&D. Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part From Federally Funded Research*, 75 Tul. L. Rev. 631, 636 (2000).

<sup>4</sup> *Why Do Prescription Drugs Cost So Much?* (visited June 21, 2001) <www.pharma.org> [hereinafter *Why Drugs Cost So Much*].



Taxpayer support for health care R&D is primarily coordinated by the NIH, which is comprised of 27 institutes and centers whose collective mission is to “sponsor and conduct medical research and research training that leads to better health for all Americans.”<sup>5</sup> In fiscal year 2001, the NIH received \$20.3 billion in support of its mission. In 2002, the NIH budget was roughly \$23 billion, an increase of 13.5%. This sizable increase is an indication that the Bush administration is, at it has stated, committed to continuing a five-year plan to double the budget of NIH by fiscal year 2003.<sup>6</sup>

Within the NIH, the Office of Technology Transfer (OTT) coordinates the transfer of both “intramural” and “extramural” research. Intramural research is conducted by federally-employed scientists working in government-owned laboratories. The government retains title to inventions discovered intramurally. Then, in exchange for royalty payments, the government gives to private industry licenses to develop and sell the technology. Extramural research, on the other hand, is conducted by privately-employed scientists using government grants. Much of this research is conducted in university labs. Under the Bayh-Dole Act of 1980,<sup>7</sup> title to inventions developed extramurally is held not by the government/grantor but by the university/grantee. The government nevertheless retains certain background rights in these inventions. Of the \$20.3 billion that NIH received in fiscal year 2001, \$2.4 billion, or 12%,<sup>8</sup> was allocated to in-house, intramural research, while 84% was allocated to extramural research.<sup>9</sup>

### *I.B.2. Intramural Research*

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<sup>5</sup>DEPARTMENT OF HEALTH AND HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH, NIH RESPONSE TO THE CONFERENCE REPORT REQUEST FOR A PLAN TO ENSURE TAXPAYERS’ INTERESTS ARE PROTECTED: A PLAN TO ENSURE TAXPAYERS’ INTERESTS ARE PROTECTED (July 2001) at 3 [hereinafter NIH RESPONSE].

<sup>6</sup>DEPARTMENT OF HEALTH AND HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH, PRESS RELEASE FOR FY2002 PRESIDENT’S BUDGET (Apr. 9, 2001).

<sup>7</sup>Act of Dec. 12, 1980, Pub. L. No. 96-517, 94 Stat. 3015-3028 (codified as amended at 35 U.S.C. §§200-211, 301-307 (1994)) [hereinafter Bayh-Dole].

<sup>8</sup>Department of Health and Human Services, National Institutes of Health, *NIH Investments* (visited Nov. 10, 2001) <[www.nih.gov/news/BudgetFY2002/FY2001investments.htm#introduction](http://www.nih.gov/news/BudgetFY2002/FY2001investments.htm#introduction)> [hereinafter *NIH Investments*].

<sup>9</sup>NIH RESPONSE, *supra* note 5, at 3.

In fiscal year 2001, the NIH allocated roughly \$2.4 billion to intramural research, research conducted by federally-employed scientists working in government labs. In accord with the mission of the NIH, these scientists conduct research that enhances human health. Along the way, the government may either seek patent protection for these inventions and/or engage in licensing agreements with companies interested in the drugs' commercialization.<sup>10</sup> The government may receive royalty payments for intramural discoveries that are ultimately commercialized by private industry.

The process of patenting an intramural invention is overseen by the OTT. To preserve U.S. patent rights, a U.S. patent application must be filed within one year of the official publication date or public use of an invention. To preserve international patent rights, the filing of a U.S. patent application must precede public disclosure of an invention. While in the process of securing patent rights in the invention, the OTT also engages in a review of the invention's commercial possibilities and develops a licensing approach. The OTT formally advertises its inventions to potential licensees, actively promotes the technology to companies, and ultimately negotiates on behalf of the government the terms of the license. Since the Bayh-Dole Act of 1980, the government has increased efforts to transfer inventions to private industry for commercialization, primarily through more frequent use of exclusive licensing.

Companies may obtain a license from the government to unpatented, patented or patent-pending material. The license may be either "exclusive" or "nonexclusive." Exclusive licenses limit the use of the invention to a single entity. This entity retains the sole right to make, use and sell the invention. A nonexclusive license, on the other hand, contemplates simultaneous use by multiple groups or entities. In deciding whether to

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<sup>10</sup>Bayh-Dole, *supra* note 7, at 35 U.S.C. § 207.

issue an exclusive or nonexclusive license, the OTT considers a variety of issues including, but not limited to, whether an exclusive license serves the best interests of the public, whether practical application of the invention will be achieved by a nonexclusive license, and whether an exclusive license is necessary to attract necessary financial investment. Applicants seeking an exclusive license are required to submit a business development plan in addition to a detailed justification of the aforementioned criteria. Notice of a proposed exclusive license is published in the Federal Register. Public comments must be received within 60 days of the publication. After consideration of these comments, a final decision on the exclusive license is made. The licensees are required to report at least annually on their utilization of the material. More importantly, the license is revocable for a number of reasons, including non-use of the patent, failure to comply with governing regulations or failure to satisfy public health needs.<sup>11</sup> From 1996 through 1998, 84.7% (or 514) of the licenses granted by NIH were nonexclusive.<sup>12</sup>

If the material is covered by a patent or patent application, two additional types of licenses are also available.<sup>13</sup> A “Commercial Evaluation License” grants the nonexclusive right to make and use technology for the purpose of evaluating its commercial potential. Under such a license, the company may not sell the product. These licenses are limited to a short amount of time, after which the company seeking to continue use of the material must obtain one of the other types of licenses. The final type of license is called an “Internal Use” license. This license allows for the right to make and use technology, but not the right to sell.

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<sup>11</sup> See discussion *infra* page 30.

<sup>12</sup> UNITED STATES GENERAL ACCOUNTING OFFICE, REPORT TO THE HONORABLE DUNCAN L. HUNTER, HOUSE OF REPRESENTATIVES, TECHNOLOGY TRANSFER, NUMBER AND CHARACTERISTICS OF INVENTIONS LICENSED BY SIX FEDERAL AGENCIES GAO/RCED-99-173 (June 1999) [hereinafter GAO REPORT TO HUNTER] at 7.

<sup>13</sup> Companies may obtain rights to biological materials not covered by a patent or patent application through a “Biological Materials License.” These licenses allow the company to make, use and sell commercially useful biological materials, even if patent protection for these materials will not be sought. As such, these licenses are typically nonexclusive.

Congress has, in addition, passed legislation enabling private entities to collaborate with government scientists on intramural research. The agreements that outline the contours of such research are called “Collaborative Research and Development Agreements” (CRADAs). CRADAs are and were intended to be flexible agreements, adaptable to the varied laboratory developments that give rise to them. Once a CRADA is entered into, the laboratory is obligated “to grant, or agree to grant in advance, to a collaborating party patent licenses or assignments, or options thereto, in any invention made in whole or in part by a laboratory employee under the agreement, for reasonable compensation when appropriate.”<sup>14</sup> As with all inventions discovered at least partially with taxpayer funding, the government retains certain rights to the invention.<sup>15</sup>

In 2000, the NIH disclosed 330 inventions, filed 189 patent applications, issued 120 patents and executed 185 licenses. Also in 2000, the NIH executed 109 CRADAs, of which 34 were standard and 75 were materials.<sup>16</sup> An impressive and lengthy list of the materials developed intramurally and currently available for licensing can be found online at the OTT website.<sup>17</sup> The list of available technologies is remarkable – on the date that this was written, 213 technologies pertaining to cancer alone were available for licensing.

In general, the number of licenses executed each year by the government for government-owned inventions has remained stable, while the royalties received for these inventions have increased.<sup>18</sup> In 2000, the NIH received \$52 million in royalties. In the five years spanning from 1996 through 1999, inclusive, NIH received licensing revenues totaling approximately \$150 million.<sup>19</sup> Though significant, these figures must be kept in perspective – they amount to only 1% of taxpayer spending on intramural research.

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<sup>14</sup>Stevenson-Wydler Technology Innovation Act of 1980, Pub. L. No. 96-480, 94 Stat. 2311-2320 (codified as amended at 15 U.S.C. §§ 3701-3714 (1994)), at 15 U.S.C. §3710a(c)(5)(C) [hereinafter Stevenson-Wydler].

<sup>15</sup>For a review of current complications in the government’s use of CRADAs, see U.S. DEPARTMENT OF COMMERCE, OFFICE OF TECHNOLOGY POLICY, TECH TRANSFER 2000: MAKING PARTNERSHIPS WORK (Feb. 2000) [hereinafter MAKING PARTNERSHIPS WORK].

<sup>16</sup>Office of Technology Transfer (visited July 3, 2001) <<http://ott.od.nih.gov/>>.

<sup>17</sup>See *id.* at <<http://ott.od.nih.gov/db/tech.asp>>.

<sup>18</sup>GAO REPORT TO HUNTER, *supra* note 12, at 4.

<sup>19</sup>NIH RESPONSE, *supra* note 5, at 6.

Law provides that federal inventors must receive the first \$2,000 of income received by the agency and then at least 15% thereafter, up to a maximum of \$150,000 per year in royalties from each licensed technologies that they invented.<sup>20</sup> In 2000, 28 NIH inventors received the maximum \$150,000 royalty.<sup>21</sup> The remaining income goes to the Institute or Center within which the licensed technology was originally developed. The funds can be used for a variety of enumerated purposes that run consistent with the general mission of NIH.

### *I.B.3. Extramural Research*

Extramural research is that conducted by non-federal employees supported by government grants. Extramural research may be conducted by institutions of higher education, research institutes and foundations, and other nonprofit and for-profit organizations. Under the terms of the Bayh-Dole Act, title in inventions discovered through extramural research rests not with the government but with the grantee. The government nevertheless retains certain rights to the invention: The government retains the right to use the invention on or for its own behalf; the grantee is required to comply with certain reporting requirements; and, the government retains the right to “march-in” on the license-holder’s property right if the license-holder has failed to meet one of a number of enumerated standards. These rights are explored in detail in the following section of the article. The NIH provides some guidance to grantees concerning their obligations under this complex regulatory framework. An online service called “Interagency Edison” has been established to, among other things, provide guidance on the reporting processes mandated by 37 C.F.R. § 401 (1995).<sup>22</sup>

The NIH spent roughly \$17 billion, or 84%, of its 2001 budget on extramural research.<sup>23</sup> Of this total,

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<sup>20</sup>The NIH has adopted a policy under which inventors receive 25% of the income after \$50,000 is attained, up to the statutory maximum. NIH RESPONSE, *supra* note 5, at 6.

<sup>21</sup>*Id.*

<sup>22</sup>See <[www.iedison.gov](http://www.iedison.gov)>.

<sup>23</sup>NIH RESPONSE, *supra* note 5, at 3.

\$11.8 billion were spent on Research Project Grants (RPGs).<sup>24</sup> RPGs are the most common funding mechanism at NIH. They are typically initiated by a researcher’s request for funding for a specific research inquiry. The NIH generally commits to providing support for an average of four years.

The priorities driving NIH grants comport with the agency’s overall mission to “expand fundamental knowledge about the nature and behavior of living systems, improve and develop new strategies for the diagnosis, treatment, and prevention of disease, reduce the burdens of disease and disability, and assure a continuing cadre of outstanding scientists for future advances.”<sup>25</sup> More specifically, programming and management decisions are based on several fundamental principles. It is worth quoting these principles at length:

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<sup>24</sup>*NIH Investments*, *supra* note 8.

<sup>25</sup>*Id.*

These priorities are set through a variety of mechanisms that take advantage of the technical and general knowledge of both federal and non-federal scientists. Mechanisms for obtaining this input include review groups, Institute or Center National Advisory Councils, conferences, workshops, *ad hoc* advisory groups, the Advisory Committee to the Director, NIH, the NIH Director's Council of Public Representatives, and the results of the Government Performance and Results Act.<sup>27</sup>

### **I.C. History of Technology Transfer**

*The government's approach to tech transfer is in a near constant state of flux. Since World War II, when the government recognized that its involvement in the wartime economy resulted in its holding a number of significant technologies, tech transfer has been the subject of steady review and debate. This section of the article provides a brief overview of the historical developments leading to today's approach to technology transfer.<sup>28</sup> Five themes emerge from this review of law and policy. First, transfers of taxpayer-funded assets from the public sector to the private sector have been taking place on terms increasingly favorable to the latter. (The debate over whether this is a positive or negative development is, for the moment, set aside.) Second, I argue that this trend may be partially attributed to our legal regime's embrace of strong property rights and a sharp public-private distinction. Third, the foreign policy implications of how government-funded inventions reach the marketplace have received alarmingly little attention. Fourth, just as the nature of R&D is continually changing, so too is the policy of technology transfer. Fifth, tech transfer policy has succeeded in stimulating the commercialization of an astounding number of new medications – the policy has, since the passage of the Bayh-Dole Act of 1980, been widely regarded as a success.*

#### *I.C.1. The Legal Backdrop*

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<sup>27</sup>*Id.*

<sup>28</sup>For a more detailed historical review, see Eisenberg, *supra* note 1, at 1671.

The arguments that shape policy development exist within a legal framework that both defines the meaning of terms and assigns these terms either positive or negative valences. For this reason, it is important to locate within this legal regime two legal doctrine that have played significant roles in shaping technology transfer policy: property law and the public-private distinction. Current policy, it may be argued, is the predictable result of a legal framework in which, first, property law favors strong property entitlements, and, second, a rigid public-private distinction clearly distinguishes entities that are public – the government – from those that are private – universities, foundations, and industry.

#### I.C.1.a. Property Law

The American legal system has for a long time vested in property holders very strong property entitlements. Indeed a fundamental tenet of 19<sup>th</sup> century property law was the premise that a property owner’s right to use and enjoy property is absolute. Similarly strong entitlements have been granted to owners of intellectual property. As previously mentioned, Congress provides an incentive to innovation by securing to investors and inventors a patent – a property right – in their inventions.<sup>29</sup> In accord with the legal regime’s general disposition toward property rights, the rights of the patent holder are very strong. In the American system, patents are limited in their duration, but, during their existence, not in their strength. A different legal regime, such as one that featured weaker property rights, might prefer an alternate approach. It may reach the same result, namely, innovation, with a patent regime that features longer patent terms but, during the term, weaker property rights. Or, a legal regime that disfavors property rights might reward inventors with

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<sup>29</sup>The Constitution authorizes the Congress “To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.” U.S. CONST. art I, §8 cl 8.



a lump-sum payment and then make the invention widely available for public consumption.

As will be discussed in detail, tech transfer proscribes a system where the government, universities and industry retain certain rights to inventions produced in collaboration with each other. These rights are typically set forth not in the background common law of property, but in contracts signed by participating parties. The grant by the government of an exclusive license, for example, is a contract in which the government retains certain rights to the property. Nevertheless, the following review of the policy's history reveals that many arguments put forward in the policy debate speak to the importance of strong property rights. Thus even though the government retains rights to the transferred property through contract, industry and universities allege that exercise of these contract rights threaten their own strong property rights in the patented invention. Unless one is cognizant of the legal framework within which the policy is developing – namely, a framework that has historically embraced strong property entitlements – it is difficult to understand why such arguments have been taken as seriously have they have been.

#### *I.C.1.b. The Public-Private Distinction*

Tech transfer policy has also been shaped by the American legal regime's longstanding adherence to a rigid public-private distinction. In the early 1800s, the law barely distinguished "public" entities from "private" entities. There was, for example, no legal distinction between the incorporation of a for-profit enterprise and the incorporation of a city or municipality. Over the years, a very rigid distinction has, for legal purposes, been elaborated. Indeed the distinction is black or white. Cities, of course, are considered "public;" for-profit entities are "private." There is no gray area in between.

*The implications that the rigid public-private distinction has on the development of technology transfer policy*

*are twofold. First, the rigid distinction makes it virtually impossible for policy-makers to conceptualize granting property rights to a single entity consisting of both public and private elements. Current policy distinguishes public entities from private entities and then focuses on the “transfer” of the property from the former to the latter. Were the public-private distinction less rigid, it might be possible for policy-makers to instead construct a joint entity which combines “public” and “private” parts. (The CRADA, incidentally, represents a small step in this direction.) Such a mixed entity might more accurately reflect the fact that the R&D process is, in reality, a collaboration among entrepreneurs, investors, scientists, universities and government employees. Its funding also comes from a full range of sources: government, universities, private industry and foundations. As will be seen, the idea of vesting property rights in this type of joint entity is never, the entire history of tech transfer policy, given serious consideration.*

Second, the rigid public-private distinction leads us, for legal purposes, to think of this complex, collaborative process as a simple “transfer” of an asset from public to private. Once the transfer has occurred and the invention is thought to be in private hands, the private sector is then able to take advantage of the full power, rhetorical and otherwise, of the legal regime’s preference for strong property rights. In this way, the two legal doctrine work together to create a disconnect between what is actually happening and the legal arguments that explain what is happening. In actuality, the R&D process is collaborative in nature and both public and private entities possess rights, through contract, in the subject invention. In legal terms, however, a property right is “transferred” from public to private hands. Any exercise of the public’s retained rights to the property threatens to blur the rigid line between public and private. The exercise of these rights also threatens the strong property rights of the private entity to whom the invention has been transferred. Together, then, property law and the public-private distinction work in tandem to secure to private entities a presumed strong entitlement to the property transferred to them.

An interesting corollary is the landmark case of *Lloyd Corp v. Tanner*.<sup>30</sup> *Here the U.S. Supreme Court grappled with the intersection of strong property rights and the public-private distinction, as well as the First Amendment. At issue was whether leafletters can exercise their First Amendment rights to expression at a shopping mall. Adhering to the rigid public-private distinction, the Court held that the shopping mall is “private” (despite the fact that the mall opens itself up to the general public and plays a role in society that, arguably, resembles that of a public square). Thus, the Court held, the property owner could exercise his strong property rights and exclude leafletters just as he can exclude any trespasser. In other words, the Court first used the public-private distinction to clearly delineate that which is private from that which is public; then, the Court found that that which is private is entitled to strong property rights. A similar result has been obtained by the policy-makers who have, over the past 50 years, been responsible for the development of tech transfer policy.*

### *I.C.2. From World War II to the Bayh-Dole Act of 1980*

During World War II, increased government outlays led to remarkable growth in the industrial capacity of the United States. Anticipating that the government’s increased role in R&D would give rise to issues concerning patents, ownership and commercialization, President Roosevelt created by executive order the National Patent Planning Commission.<sup>31</sup> The Commission analyzed the role that patents play in government-funded research and, in a report issued in 1945, determined that a balance must be struck between, on the one hand, keeping public inventions in the public domain, and, on the other, allowing for their private ownership.<sup>32</sup> According to commentator Rebecca Eisenberg, the primary concern of the Commission was

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<sup>30</sup>*Lloyd Corp. v. Tanner*, 407 U.S. 551 (1972).

<sup>31</sup>2 Subcommittee on Domestic and Int’l Scientific Planning and Analysis of the House Committee on Science and Technology, 94<sup>th</sup> Cong., Background Materials on Government Patent Policies: Reports of Committees, Commissions, and Major Studies xi (Comm. Print 1976) [hereinafter Background Reports].

<sup>32</sup>National Patent Planning Commission, Government-Owned Patents and Inventions of Government Employees and Con-

to ensure that the government itself protects its own ability to use taxpayer-funded inventions. Beyond that, the Commission indicated a preference for the free and open use of government-funded inventions by anyone. There was, thus, a presumption in favor of nonexclusive licensing. Exclusive licensing, by contrast, was recommended only when necessary to induce private manufacturers to engage in further R&D and commercialization.<sup>33</sup> To this end, the Commission recommended that government agencies “issue exclusive licenses in cases where it seems evident that otherwise the inventions in question will not come into general use.”<sup>34</sup>

Agencies proceeded to take varied approaches to tech transfer activity. Some followed a “title” policy that called for the government to retain title in its own inventions. This approach comports with the philosophy that public inventions should remain in the public domain.<sup>35</sup> Agencies taking this approach included the Department of Agriculture<sup>36</sup> and the Department of Health, Education, and Welfare (HEW).<sup>37</sup> Other agencies took a “license” approach. Under this approach, which was advocated in a 1947 report by the Attorney General,<sup>38</sup> the government retains certain rights, including a license to use the invention on its own behalf, but otherwise transfers title in the invention to the contractor. Most notably, this approach was taken by the DoD.<sup>39</sup>

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tractors, reprinted in Background Reports, *supra* note 31 (1945) [hereinafter Patent Planning Commission].

<sup>33</sup>Eisenberg, *supra* note 1, at 1672.

<sup>34</sup>Patent Planning Commission, *supra* note 32, at 4-5.

<sup>35</sup>Despite their interest in developing the public domain, proponents of the title approach nevertheless favored the patenting of government inventions by the government itself. *See* Eisenberg, *supra* note 1, at 1675.

<sup>36</sup>Agriculture Research and Marketing Act of 1946, 7 U.S.C. § 427i(a) (1994).

<sup>37</sup>James A. Dobkin, *Patent Policy in Government Research and Development Contracts*, 53. Va. L. Rev. 564 (1967) at 580.

<sup>38</sup>ATTORNEY GENERAL OF THE UNITED STATES, INVESTIGATION OF GOVERNMENT PATENT PRACTICES AND POLICIES: REPORT AND RECOMMENDATIONS OF THE ATTORNEY GENERAL TO THE PRESIDENT, partially reprinted in Background Reports, *supra* note 31, at 15 (1947).

<sup>39</sup>Dobkin, *supra* note 37, at 574.

In the 1960s, the Kennedy administration continued to balance government retention of rights with incentives for private development, while at the same time attempting to standardize the policy across government agencies. A 1963 Presidential Memorandum and Policy Statement identified circumstances wherein the government would retain title in the invention, but, at the same time, continued to allow heads of agencies to grant at their discretion an exclusive license where necessary “to call forth private risk capital and expense.”<sup>40</sup> Agency heads acted upon this discretion to grant exclusive licenses only rarely – nonexclusive licensing was the general rule.

The Presidential Memorandum notwithstanding, agencies continued to vary in their approaches to technology transfer. In 1962, for example, the NIH began to require significantly more of private industry than did other agencies. Specifically, the NIH required private entities to sign an extensive agreement with the agency prior to screening for biological activity compounds developed with NIH funds. The agreement restricted the ability of firms to disclose the results of their testing, obligated the prompt reporting to the government of results, restricted the firms’ rights to obtain patents on new uses, and retained for the government a nonexclusive license.<sup>41</sup> These stringent requirements dampened private interest in the development of public inventions. The NIH policy did not change until 1968.<sup>42</sup> After 1968, NIH policy enabled, among other things, institutions of higher education to patent inventions discovered under government grants.<sup>43</sup> The universities could then sell exclusive rights to these patented products to private industry. Thus the university would get royalties, but not the government. A strikingly similar policy was later to be adopted by Congress in

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<sup>40</sup>Memorandum and Statement of Government Patent Policy, 28 Fed. Reg. 10,943 (1963) at 10,944.

<sup>41</sup>2 Harbridge House, Government Patent Policy Study, Final Report for the FCST Committee on Government Patent Policy (1968) at 12-13 [hereinafter Harbridge House Report].

<sup>42</sup>COMPTROLLER GENERAL OF THE UNITED STATES, REPORT TO THE CONGRESS: PROBLEM AREAS AFFECTING USEFULNESS OF RESULTS OF GOVERNMENT-SPONSORED RESEARCH IN MEDICINAL CHEMISTRY, reprinted in 1 Government Patent Policies: Institutional Patent Agreements: Hearings Before the Subcomm. on Monopoly and Anticompetitive Activities of the Senate Select Comm. on Small Bus., 95<sup>th</sup> Cong. 373-98 (1978) at 109.

<sup>43</sup>Eisenberg, *supra* note 1, at 1683.

Bayh-Dole.

In 1965, the Federal Council for Science and Technology (FCST), a division of the executive branch, commissioned Harbridge House, a leading consulting firm with expertise in science and technology, to conduct a study on the government's patent policy.<sup>44</sup> Published in 1968, the Harbridge House Report found that the rate of commercial utilization of government inventions was low.<sup>45</sup> Although many used this finding to argue that greater use of exclusive licensing was necessary to commercialize government inventions, the Report itself did not find the evidence sufficient to resolve this debate. The Report stated that "the evidence does not indicate that either title or nonexclusive licensing is uniformly the best way to promote utilization."<sup>46</sup> The Report did, however, note that exclusive licensing may be necessary "where the invention is commercially oriented but requires substantial private development to perfect it, applies to a small market, or is in a field occupied by patent sensitive firms and its market potential is not alone sufficient to bring about utilization."<sup>47</sup>

In a 1971 Presidential Memorandum, the Nixon administration largely implemented the recommendations of the Harbridge House Report.<sup>48</sup> Eisenberg explains that the Memorandum "facilitated the allocation of exclusive rights in government-sponsored inventions in a number of ways. They clarified the authority of government agencies to grant greater rights than a nonexclusive license... They allowed agencies to revoke nonexclusive licenses held by contractors in order to grant exclusive licenses where necessary to encourage

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<sup>44</sup>Harbridge House Report, *supra* note 41, at ii.

<sup>45</sup>Specifically, the Report found that only 12.4% of a sample of government-sponsored inventions that were patented in the years 1957 and 1962 had actually been put to use. *See id.*, at 3-4.

<sup>46</sup>*Id.*

<sup>47</sup>*See id.*, at vii.

<sup>48</sup>Memorandum and Statement of Government Patent Policy, 36 Fed. Reg. 16,887 (1971).

commercialization of the invention. Finally, they explicitly authorized exclusive licenses under government-owned patents.”<sup>49</sup>

Thus from WWII to the 1970s, technology transfer slowly shifted toward greater use of exclusive licenses. This meant that the executive branch had been transferring government-funded inventions to private entities on terms increasingly favorable to the latter, largely without congressional approval or oversight. The executive branch’s policy involved transfers of assets worth millions of dollars, including assets such as essential medicines and military technology. Such transfers, it was increasingly believed, required congressional approval, and interest in congressional action began to grow. Several lawsuits were brought in the early 1970s challenging the constitutional authority of the executive branch to transfer taxpayer-funded inventions without express statutory authorization.<sup>50</sup>

Calls for congressional action were also coming from universities, private industry and even the executive branch itself. After years of adjusting to new administrations and new heads of agencies, universities and private industry sought some measure of policy stability. The NIH, for example, threatened in 1978 to return to the stricter policies of the 1960s. And then, in 1979, President Carter voiced support for more extensive exclusive licensing as part of his plan to invigorate industrial productivity.<sup>51</sup> At this time, there existed a growing sentiment that the United States had lost its position as the global leader in technological innovation. Japan in particular was mounting a vigorous campaign to claim the technology throne. An address on the topic that President Carter made to Congress provided the impetus for congressional action.

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<sup>49</sup>Eisenberg, *supra* note 1, at 1685.

<sup>50</sup>The courts never reached decisions on the merits, as these lawsuits were dismissed for lack of standing. *Public Citizen v. Sampson*, 180 U.S.P.Q. (BNA) 497 (D.D.C. 1974); *Public Citizen v. Sampson*, 379 F. Supp. 662 (D.D.C. 1974).

<sup>51</sup>Industrial Innovation Initiatives: Message to Congress on Administration Actions and Proposals, PUB. PAPERS 2070, 2071 (Oct. 31, 1979). Carter’s address was largely based on the findings of the Domestic Policy Review Final Report. Advisory Committee on Industrial Innovation, Industrial Advisory Subcommittee on Patent and Information Policy, Report on Patent Policy (1979), reprinted in *Advisory Committee on Industrial Innovation: Final Report* (1979).

This action, which came to be known as the Bayh-Dole Act, placed a congressional stamp of approval on the direction in which technology transfer policy had been moving, namely, increased use of exclusive licenses.

### *I.C.3. The Bayh-Dole Act of 1980*

The Bayh-Dole Act of 1980<sup>52</sup> is widely credited with having ushered in the modern era of technology transfer policy. The Act signaled broad congressional approval of exclusive licensing, with several taxpayer protections built into the bill to protect against abuse of these licenses. Commentators have described its impact as marking a “sea change” in the policy.<sup>53</sup> Exclusive licenses had been rare under Kennedy, and still quite rare under Nixon. Now, agencies had a congressional green light to more aggressively pursue exclusive licensing where necessary to induce commercialization.

Congress actually passed two significant pieces of legislation in 1980 pertaining to technology transfer. The Bayh-Dole Act concerns itself with extramural R&D. Extramural R&D is that conducted by private institutions (such as universities, foundations and for-profit companies) using government funding. The Stevenson-Wydler Act, on the other hand, concerns itself with intramural research, or, research conducted by federal scientists in state-owned labs.<sup>54</sup> I will first discuss Bayh-Dole.

The objectives of Bayh-Dole indicate that Congress intended to grapple with the same issues that had been driving technology transfer policy since World War II, namely, how to balance the value of keeping publicly-funded inventions in the public domain with the need to grant exclusive licenses to induce commercialization.

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<sup>52</sup>Bayh-Dole, *supra* note 7.

<sup>53</sup>Eisenberg, *supra* note 1, at 1663. The Act has also been referred to as a “major departure” from existing agency practice. Arno & Davis, *supra* note 3, at 646.

<sup>54</sup>Stevenson-Wydler, *supra* note 14.



The objectives of the Act are:

to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area. 35 U.S.C. § 200.

Curiously absent from this description of the Act's purpose is mention of a major issue weighing heavily on the minds of legislators – ensuring that American business remained on par or ahead of foreign competition. At this time, Japan had surpassed Silicon Valley as the world's leader in superconductor design and manufacturing. There was grave concern that America had lost its technological superiority. Senator Birch Bayh, for example, opened a Senate hearing on the Act by stating that he had “become very concerned that the United States is rapidly losing its preeminent position in the development and production of new technologies.”<sup>55</sup> He goes on to note that “importation of foreign manufactured goods are second only to foreign imported oil as the biggest drain on U.S. dollars.”<sup>56</sup> Senator Bob Dole stated that the purpose of the Act was to ensure that the U.S. government played a more direct role in stimulating technological advance: “The development of technological innovation by government and industry in countries such as Japan and Germany is a contributing factor in their dominance of world trade.”<sup>57</sup> Though absent from the Act's final language, it is clear that a central purpose of the legislature was to stimulate R&D.

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<sup>55</sup> *The University and Small Business Patent Procedures Act, Hearings Before the Committee on the Judiciary, United States Senate, on S. 414*, 96<sup>th</sup> Cong., 96-11 (May 16, and June 6, 1979) [hereinafter *Senate Hearings*] at 1 (opening statement of Senator Birch Bayh).

<sup>56</sup> *Id.*

<sup>57</sup> *See Id.*, at 28 (opening statement of Senator Bob Dole)

Bayh-Dole promotes the use of exclusive licensing to ensure commercialization of taxpayer-funded inventions. Small businesses and universities using federal funding are entitled under the Act to retain title to inventions. A university can, in turn, license that invention to businesses, large or small, interested in commercializing the product. In exchange for an exclusive license to the invention, universities receive up-front payments and/or royalties.

Although the Act enables title to vest in small businesses conducting R&D with government funds, it is silent as to whether title can vest in large businesses. Fearing that voters would view such a policy as a handout to big business, legislators determined that inclusion of big business in the Act was a political liability. An amendment to include large businesses failed in the Senate by a vote of 60-34.<sup>58</sup> Big business had lobbied vigorously for their inclusion in the bill, and many felt that their exclusion might cause agencies that had previously allowed title to vest in big business to change their policy. This fear was not to be realized, as agencies continued their existing practice of allowing large businesses to retain title to inventions. These agency practices received express approval when, by executive order, President Ronald Reagan extended the provisions of Bayh-Dole to big business in 1983.<sup>59</sup>

A significant number of legislators were concerned that the exclusive licenses might be abused. Thus three types of provisions designed to protect taxpayers from such abuses were ultimately included in the Act. First, the government retained for itself the right to use the invention for or on its own behalf.<sup>60</sup> Second, the grantee is required to comply with reporting procedures. These call for the grantee to notify the government

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<sup>58</sup>Letter from Sen. Gaylord Nelson, Chairman, Senate Select Comm. on Small Bus., to Rep. Robert w. Kastenmeier, Chairman, Subcomm. on Courts, Civil Liberties, and the Admin. of Justice of the House Comm. on the Judiciary (June 9, 1980), reprinted in *Industrial Innovation and Patent and Copyright Law Amendments: Hearings on H.R. 6933* [misabeled as 6033], *H.R. 6934*, *H.R. 3806*, *H.R. 2414* (*The President's Industrial Innovation Program*) before the Subcomm. on Courts, Civil Liberties, and the Admin. of Justice of the House Comm. on the Judiciary, 96<sup>th</sup> Cong. 286(1980) [hereinafter *House Hearings*] at 877-78

<sup>59</sup>Memorandum to the Heads of Executive Departments and Agencies: Government Patent Policy, PUB. PAPERS 248 (Feb. 18, 1983). Similar policy was given further Presidential approval through an Executive Order signed in 1987. Exec. Order No. 12,591, 52 C.F.R. 13414 (1987).

<sup>60</sup>Bayh-Dole, *supra* note 7, at 37 C.F.R. § 401.14(b).

of any invention within two months of disclosure to the grantee’s employees.<sup>61</sup> Then, the grantee must again notify the agency within two years as to whether it wishes to exercise its title to the invention.<sup>62</sup> Should the grantee fail to meet these reporting deadlines, the government may, upon submission of a written request to the grantee, assert its own title to the invention.<sup>63</sup> Importantly, the Act further requires that a legend be placed on both the patent application and any resulting patent that identifies the invention as a product of taxpayer dollars.<sup>64</sup>

The third taxpayer protection included in Bayh-Dole is the government’s retained “march-in rights.” These provisions entitle a funding agency to issue nonexclusive licenses or to require a contractee or exclusive licensee to grant nonexclusive licenses to other applicants if the agency determines that:

- “(1) Such action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps *to achieve practical application* of the subject invention in such field of use;
- (2) Such action is necessary *to alleviate health or safety needs* which are not reasonably satisfied by the contractor, assignee or their licensees;
- (3) Such action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee or licensees; or
- (4) Such action is necessary because the agreement required by paragraph (i) of this clause has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of such agreement.” 37 C.F.R. § 401.14(j) (emphasis added).

The term practical application is defined as:

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<sup>61</sup>Bayh-Dole, *supra* note 7, at 37 C.F.R. § 401.14(c)(1).

<sup>62</sup>Bayh-Dole, *supra* note 7, at 37 C.F.R. § 401.14(c)(2).

<sup>63</sup>Bayh-Dole, *supra* note 7, at 37 C.F.R. § 401.14(d).

<sup>64</sup>Bayh-Dole, *supra* note 7, at 37 CFR 401.14(c)(3).

“to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are, to the extent permitted by law or government regulations, available to the public on *reasonable terms*.” 37 C.F.R. § 401.14(a)(3) (emphasis added).

The march-in rights were intended to prevent two outcomes: First, where a private entity sits on a taxpayer-funded invention and fails to commercialize it in a timely fashion; and, second, where a private entity takes advantage of the exclusive license and charges an unreasonable price for the product. Although no specific formula was put forward to calculate what constitutes an unreasonable price and profit, it is fair to say that the march-in provisions were intended to protect against corporate windfalls. Of course, the Act certainly contemplated some return on investment, for such a return is necessary to induce commercialization.

The effectiveness of these three taxpayer protections has been and continues to be the subject of heated debate. It has been argued that the government rarely uses a product on its own behalf; that the reporting requirements are ineffective; and, that the march-in provisions have *never* been utilized. A comprehensive analysis of these concerns is presented in Section II.

In 1980, Congress also passed the Stevenson-Wydler Act.<sup>65</sup> Whereas Bayh-Dole addresses extramural research, Stevenson-Wydler addresses intramural research. The legislation enables and encourages government agencies to execute exclusive licenses with private actors to encourage commercialization of inventions. The Act provides a financial return to taxpayers primarily in the form of royalty payments, which go to both the individual inventor as well as the funding agency. In 1986, the Stevenson-Wydler approach to intramural development was augmented by the Federal Technology Transfer Act, which authorized federal researchers to collaborate with private actors through the use of CRADAs.

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<sup>65</sup>Stevenson-Wydler, *supra* note 14.

#### *I.C.4. Perspectives on Policy Developments*

Five significant themes emerge from even this brief overview of the history of tech transfer. The first is that there has been a trend over time to transfer taxpayer assets from public to private hands on terms increasingly favorable to the latter. Early debates over whether to use exclusive licenses have all but disappeared. Their use is now widely accepted, and instead policy-makers debate how to build taxpayer protections into the background rights of such licenses. (As will be seen in Section II, the debate over these taxpayer protections can be intense.)

*Second, technology transfer policy has been influenced by the legal regime in which it has developed. Specifically, the rigid public-private distinction clearly distinguishes public entities from private entities and leads policy-makers to place the drug, at any one time, in the hands of either one or the other. Then, the entity in possession of the drug can take advantage of the legal regime's preference for strong property rights. The result is a policy that resembles a relay race. Government – the public – runs the first leg when it engages in basic, foundational research. Industry – the private – runs the second leg when it conducts clinical trials and achieves commercialization. Tech transfer policy exists to ensure that the baton, the drug, is cleanly transferred from the public to the private. When industry runs the second leg, it alone has possession of the baton (and can therefore take advantage of the legal regime's preference for strong property rights). During the second leg, exercise by the government of its retained rights to the baton would appear to violate the rules of the race. However, the relay race conceptualization of the drug development process is an oversimplification. Scientists work together, funds are co-mingled and intellectual property rights are granted by, retained by, and enforced by the government. Policy-makers should not let the legal regime's posture toward property rights and the public-private distinction oversimplify, for legal purposes, what is in reality a complex and collaborative process.*

The third interesting element of policy development is what is absent: adequate consideration of its international, foreign policy implications. The legislators who passed Bayh-Dole were concerned about foreign competition – they wished to ensure that America reemerged as the global leader in technology. Tech transfer, however, affects not only international competition but also international equity and global security. The U.S. government plays a formative role in the development of critical pharmaceutical medications and dangerously effective pieces of military equipment, yet, American citizens have little to no control over how these inventions enter the international marketplace. For example, American citizens helped to develop Zerit, an effective AIDS medication. In the face of a growing AIDS epidemic in Africa, private industry, the second runner in the relay race, priced this medication out of the reach of African patients. Regardless of whether this price is justifiable and regardless of whether U.S. citizens had any say in the pricing strategy, the latter are held accountable, in the international arena, for how their inventions entered the marketplace. When African AIDS patients and their families discover the role that U.S. citizens played in the development of a medication to which they were effectively denied access, what attitudes toward America might we expect them to harbor?<sup>66</sup>

*Fourth, one must not let the significant impact of Bayh-Dole obscure the fact that technology transfer policy is flexible and evolutionary in character. Just as the nature of R&D changes over time, so too will the nature of tech transfer. The legislature may step in from time to time (as it did in 1980), but many of the changes in policy have been and will continue to be made piecemeal by the executive branch. Despite progress toward greater standardization across agencies, agencies continue to wield a significant amount of discretion over the terms of asset transfers. A recent government report highlights this notion, finding as one of its “major insights” the fact that “generic procedures for partnering and licensing provided by the federal*

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<sup>66</sup>This issue recently emerged at the WTO negotiations in Doha, Qatar, when poorer countries demanded flexibility in the international patent regime to respond to health crises. The negotiations did not distinguish products developed entirely with private investment from those partially funded by public. See discussion *infra* page 87.

*laws have taken on different shapes as they have been integrated into the distinctive research missions of the agencies.”<sup>67</sup> Whether to exercise march-in rights, for example, is an important decision that is made at the agency level.*

Fifth, and finally, the technology transfer regime proscribed by Bayh-Dole is now widely regarded as a success. The security afforded by exclusive licenses has encouraged private industry to invest in government-funded technologies and risk bringing them to the market. And to the market they have come – doctors now have a much wider array of medicines and equipment to choose from, enabling patients to lead longer and healthier lives. The forces driving this explosion in health care technology are numerous, but among them, many believe, is technology transfer. Even critics of tech transfer concede that Bayh-Dole has succeeded in giving business adequate incentive to commercialize government-funded inventions. As will be seen in the following section, their concern is rather that the policy has gone too far.

## II.

### Current Policy Debates

The Bayh-Dole regime is widely regarded as a success. This section begins with a presentation of the arguments supporting this conclusion. These arguments then form the backdrop against which the three most significant critiques of current policy are measured. The three questions currently raised by critics of tech transfer policy can be categorized as follows: Are exclusive licenses absolutely necessary to ensure commercialization of government-funded inventions? Are taxpayers maximizing the return on their investment

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<sup>67</sup>MAKING PARTNERSHIPS WORK, *supra* note 15, at 5.

in R&D? And, is the policy facilitating R&D with the greatest potential to maximize human health and welfare? The section concludes with several perspectives on these current debates. I argue, among other things, that a lack of information is hampering the effective resolution of all three issues.

## II.A. The Success of the Bayh-Dole Regime

Since 1980, the number of medicines and health care technologies reaching the marketplace has skyrocketed. University scientists are increasingly focused on the potential commercial applications of their research. Hundreds of biotech firms are now busily conducting clinical tests on government-funded inventions, whereas thirty years ago virtually no such small biotech firm existed. This activity means that doctors now have a much wider array of medicines and equipment to choose from, enabling patients to live longer and healthier lives. PhRMA calls the recent advances in medicine “unprecedented” and “nothing short of remarkable.”<sup>68</sup> Among the many forces driving this progress is the Bayh-Dole regime of technology transfer.<sup>69</sup> The regime encouraged the use of exclusive licenses to government-funded inventions, providing private industry with the security and financial incentive necessary to invest in the risky and expensive drug development process.

The Tufts Center for the Study of Drug Development, an independent research organization wholly funded by pharmaceutical companies, announced in November 2001 that the cost of developing a pharmaceutical medication is \$802 million.<sup>70</sup> This figure represents the *total* cost of developing a new drug, including basic,

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<sup>68</sup> *Why Drugs Cost So Much*, *supra* note 4.

<sup>69</sup> Other significant forces driving the explosion in biomedical technology are the insights and technical capacity generated by recent scientific breakthroughs. Among these breakthroughs is the ability to replicate compounds that, until recently, could only be produced through natural processes.

<sup>70</sup> TUFTS CENTER FOR THE STUDY OF DRUG DEVELOPMENT, TUFTS CENTER FOR THE STUDY OF DRUG DEVELOPMENT PEGS COST OF A NEW PRESCRIPTION MEDICINE AT \$802 MILLION (Nov. 2001). This report follows the same method and uses the same assumptions as a report that the Tufts Center released in 1991 pegging the cost at \$231 million (in 1987 dollars). Had the costs kept pace with inflation, the new cost would have been \$318 million (in 2000 dollars). The Tufts Center attributes the significant rise in costs to the increased cost of conducting clinical trials. The Tufts Center receives 65% of its budget in donations from pharmaceutical companies. The remaining 35% consists of revenues collected largely from pharmaceutical companies in exchange for copies of the Center’s reports and publications.



foundational research, clinical testing, and the approval process. As previously discussed, the government tends to pay for the early stages of drug development, private industry the later. The study's methodology was thoroughly analyzed and largely corroborated by a government study.<sup>71</sup>

The Tufts Center figure incorporates three elements: "out-of-pocket expenditures" account for 10% of the cost, "risk" accounts for 20-25%, and "opportunity cost of capital" accounts for roughly 65%. "Out-of-pocket expenditures" cover preclinical research, clinical testing and the regulatory filings necessary for FDA approval. "Risk" accounts for the fact that significant amounts of money are spent on drugs that ultimately fail. According to PhRMA, 99.9% of tested drugs never even begin clinical trials, and only 20% of drugs that begin clinical testing emerge as commercially-viable, FDA-approved pharmaceuticals.<sup>72</sup> "Opportunity cost of capital" accounts for the fact that drugs take a long time to develop, and, during that time, the corporation could have invested in other projects.

Because the FDA has come to require increasingly stringent clinical testing, out-of-pocket expenditures, risk and opportunity cost of capital have each escalated. Perhaps when the approval requirements were looser, industry might have commercialized a government-funded invention with only a nonexclusive license. But, such is not the case today. Today, absent the security of an exclusive license, industry simply would not risk their capital commercializing a government-funded invention. Conventional wisdom maintains that Bayh-Dole, in securing to industry the exclusive licenses necessary to incentivize commercialization, helped to stimulate the explosion in biomedical progress that now brings greater health benefits to everyone.

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<sup>71</sup>OFFICE OF TECHNOLOGY ASSESSMENT, PHARMACEUTICAL R&D: COSTS, RISKS AND REWARDS, OTA-H-522 (1993). Roughly half of the \$802 million figure is the so-called opportunity cost of capital – the profit that industry could return were they to expend their money on other projects. This figure incorporates the costs expended on the many drugs that fail to emerge from either initial testing or clinical testing.

<sup>72</sup>Raquel Pontes de Campos, *AIDS: The great divide. Dispute over generic drugs pits the world's haves against have-nots*, THE SEATTLE TIMES, June 13, 2001, at A3.

## II.B. Three Current Questions

Although Bayh-Dole is widely heralded as a success, the policy is not without critics. Current controversies over tech transfer can be categorized into three questions.

### *II.B.1. Are Exclusive Licenses Necessary to Ensure the Commercialization of Government-Funded Inventions?*

One challenge to the conventional wisdom regarding Bayh-Dole comes from those who question whether exclusive licenses are in fact necessary to incentivize commercialization of government-funded inventions. These individuals concede that exclusive licenses stimulate commercialization of government-funded inventions. Nevertheless, these advocates contend that it may be possible to achieve commercialization without going so far as to provide an exclusive license.

Proponents of exclusive licensing defend the practice by pointing not only to the successful record of commercialization in the post-Bayh-Dole era, but also the unsuccessful record of the pre-Bayh-Dole era. In the 1970s, industry argued that government-funded inventions were languishing in government labs. These arguments helped to convince legislators that expanded use of exclusive licensing was necessary to incentivize commercialization. In a hearing on the Bayh-Dole Act, Senator Bayh remarked that “agencies have had very little success attracting private industry to develop and market these inventions because when the agencies retain the patent rights there is little incentive for any company to undertake the risk and expense of trying to develop a new product.”<sup>73</sup> Proponents of this view believed that nothing short of exclusive licensing was necessary to keep government-funded inventions from being left on the laboratory floor. This view was ultimately reflected in the provisions of Bayh-Dole.

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<sup>73</sup>*Senate Hearings*, *supra* note 55, at 2 (opening statement of Senator Birch Bayh).

Professor Rebecca Eisenberg, however, has questioned the key statistic often cited by both industry and legislators in the discussions preceding Bayh-Dole. The statistic, cited here by Senator Dole, was that “of the 28,000 patented inventions partially funded by the Government, only about five percent have been used.”<sup>74</sup> First, Eisenberg notes that the patents referred to by Senator Dole were largely the product of grants from the DoD. Indeed 63% of these patents came from the DoD, and, of these patents, a mere 1% had been commercialized. Under the terms of these DoD patents, Eisenberg notes, contractors could have, had they wanted to, chosen to retain title. Their failure to do so indicates that these inventions, despite being patented, were of little commercial value.<sup>75</sup> Eisenberg further notes that only 325 of the 28,000 patents were from the HEW (now the Department of Health and Human Services (HHS)). Of these, 75 (23%) were licensed as of the end of fiscal year 1976.<sup>76</sup> Finally, Eisenberg argues that “the number of patent licenses may be a misleading measure of utilization of inventions in that it overlooks both unlicensed development of patented inventions and development or commercial utilization of unpatented inventions.”<sup>77</sup> According to the Harbridge House study, these practices were “common knowledge.”<sup>78</sup> For these reasons Eisenberg maintains that the record of commercialization in the pre-Bayh-Dole era may not have been as poor as many contend.

Aside from the statistic cited by Senator Dole and challenged by Eisenberg, there are two additional pieces of evidence that may reveal whether exclusive licenses provide a necessary incentive. First, there is evidence that the stringent HEW policies of the 1960s had a chilling impact on public-private collaboration. As

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<sup>74</sup>See *id.*, at 28 (opening statement of Senator Robert Dole).

<sup>75</sup>Eisenberg, *supra* note 1, at 1702.

<sup>76</sup>See *id.*, at 1703.

<sup>77</sup>*Id.*

<sup>78</sup>Harbridge House Report, *supra* note 41, at 7.

previously noted, the agency imposed strict reporting requirements on private entities interested in obtaining rights to government inventions, and also reserved for the government a nonexclusive license to the product. Proponents of exclusive licensing allege that public-private collaboration ground to a halt during this period primarily because of the nonexclusive licensing provision. However, despite these claims, nobody has been able to cite to a specific invention that failed to make it to the market in a timely fashion during this period. Moreover, some university and government scientists have stated that, at that time, industry was willing to commercialize products despite having only a nonexclusive license.<sup>79</sup> (The rising cost of clinical trials may mean that industry would be unwilling to do the same today.)

Second, in 1989, the NIH adopted a policy in CRADA negotiations that there should be “a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public.”<sup>80</sup> The NIH reports that this reasonable-pricing clause led many companies to withdraw from collaboration, and that the policy resulted in a “relatively flat growth rate” of CRADAs between 1990 and 1994.<sup>81</sup> If a reasonable pricing clause eliminated industry’s incentive to collaborate, then certainly, it may be argued, would a policy of nonexclusive licensing. However, contrary to the assertion of the NIH, the Office of Technology Policy (OTP) has reported that the reasonable pricing clause did *not* chill industry collaboration. Indeed the OTP trumpets the growth rate of CRADAs during the 1990s, reporting that the number of active CRADA projects with HHS grew steadily throughout the 1990s, from 110 in 1990, to 147 in 1994, to 163 in 1998.<sup>82</sup> The reasonable-pricing clause may have made investment in government-funded inventions less attractive to private industry; but, it was still attractive enough.

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<sup>79</sup>Interview with Dr. William Prusoff, Professor Emeritus, Yale University School of Medicine, in New Haven, Ct. (Jan. 17, 2002); Telephone Interview with Dr. Marc Kirshner, Chairman, Department of Cell Biology, Harvard University School of Medicine, (Feb. 7, 2002).

<sup>80</sup>NIH RESPONSE, *supra* note 5, at 9.

<sup>81</sup>*Id.*

<sup>82</sup>MAKING PARTNERSHIPS WORK, *supra* note 15, at p 92.

To summarize, the debate over whether exclusive licenses are necessary to incentivize commercialization continues to exist, though it is much less controversial than it once was. Bayh-Dole placed a heavy thumb on the scale in favor of exclusive licensing, and its success has, for the most part, quieted calls for a return to the days of nonexclusive licenses. Nevertheless, there remain commentators who argue that the pre-Bayh-Dole years may not have been as bad as proponents of exclusive licensing contend.

### *II.B.2. Are Taxpayers Maximizing the Return on Their Investment?*

A second issue raised by critics of technology transfer policy is whether taxpayers are maximizing the return on their investment in biomedical R&D. Everyone agrees that inventions must be commercialized – they should not be left to languish in government labs. Everyone also seems to agree that they should be commercialized on terms as favorable to taxpayers as possible. This mission is reflected in the terms of Bayh-Dole, which calls for agencies to transfer inventions on terms “not greater than reasonably necessary to provide the incentive” to commercialize.<sup>83</sup> Numerous commentators, while conceding that exclusive licenses may be necessary to ensure commercialization, nevertheless contend that more should be done to protect the taxpayer investment from abuses of these licenses.

Taxpayer returns come in many forms. First, commercialization enables consumers to access inventions. This is perhaps the most important return, for it directly leads to greater health. Second, sales of commercialized inventions generate tax revenue. Third, scientific progress helps drive economic growth. One government report finds that the benefit of increased life expectancy creates annual net gains of about \$2.4 trillion (in

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<sup>83</sup>Bayh-Dole, *supra* note 7, at 35 U.S.C. §209(c)(1)(A)-(D).

1992 dollars). Even if only 10% (\$240 billion) of this total is attributable to government funding, taxpayers are receiving a remarkable rate of return on the annual NIH investment of \$16 billion.<sup>84</sup>

Furthermore, taxpayers can maximize the return on their investment by ensuring for themselves a price for the medication no higher than that necessary to ensure commercialization. Industry skeptics have long been concerned that exclusive licenses might enable industry to earn a profit in excess of that which was necessary to have incentivized commercialization in the first place. Some of these excess profits might be funneled back into R&D; the rest, however, would go to shareholders. This is the so-called corporate windfall, the windfall that Bayh-Dole was designed to prevent. In a Senate hearing, for example, Senator Bayh noted that “criticism comes from those that feel that this bill is a front to allow the large, wealthy corporation to take advantage of Government research dollars and thus to profit at the taxpayers’ expense. We thought we had drafted this bill in such a way that this was not possible.”<sup>85</sup>

Legislators built three forms of taxpayer protections into the Bayh-Dole regime of tech transfer. First, the government retains a right to use government-funded inventions “on and for its own behalf.” Second, private entities taking advantage of government funding must comply with reporting requirements. And, third, the government retains the right to “march-in” on a patent if it is not being made available to the public on reasonable terms. (Provisions pertaining to a fourth protection – royalty payments – were dropped at the last moment.) Critics of current policy argue that even if these three taxpayer protections sound like enough on paper, they have failed to protect taxpayers in practice.

First, the government seldom uses licenses on and for its own behalf.<sup>86</sup> Significantly, the government has

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<sup>84</sup>THE U.S. CONGRESSIONAL JOINT ECONOMIC COMMITTEE (JEC), THE BENEFITS OF MEDICAL RESEARCH AND THE ROLE OF NIH (May 2000), quoted in NIH RESPONSE, *supra* note 5, at 10.

<sup>85</sup>*Senate Hearings*, *supra* note 55, at 44 (during Senator Bayh’s questioning of Elmer Staats, Comptroller General of the United States).

<sup>86</sup>MAKING PARTNERSHIPS WORK, *supra* note 15, at 24. *See also* GOVERNMENT ACCOUNTING OFFICE, TECHNOLOGY TRANSFER: REPORTING REQUIREMENTS FOR FEDERALLY SPONSORED INVENTIONS NEED REVISION GAO/RCED-99-242 (Aug. 12, 1999)

never attempted to use this provision to produce its own drugs, at cost, for Medicare.<sup>87</sup> Second, it is now widely recognized that reporting requirements fail to adequately protect the taxpayers' investment. The government does not know, for example, whether a specific NIH grant gave rise to a patented invention – no database links grant information to patent information. Or, consider the following fundamental questions: Of all of the new drugs approved by the FDA in 2001, how many were developed at least partially with government funds? Which ones? Surprisingly, these two questions can be neither quickly nor easily answered. One must locate the actual patents on the commercialized drugs and then search for the legend, mandated by Bayh-Dole, that labels the invention as a product of government funding. Even if such a label is found, the researcher will still have no way to track the *size* of the taxpayer investment (again because there is no database linking grant information to patent information).

More troubling, however, is the fact that the legend mandated by Bayh-Dole is often missing altogether. Bayh-Dole requires that any invention discovered with any amount of government funding include a label that recognizes the government's contribution. A review of medically related patents issued in 1997 found that 143 of a total 633 patents did not include such a label, signaling that these 143 inventions were discovered without any government funding at all. Alarming, grantees later conceded that 79 of these 143 inventions were in fact the product of government funding.<sup>88</sup> Arno and Davis write that “the failure to include a legend is a kind of insurance against discovery and, without mincing words, amounts to theft of government property and ongoing fraud of massive proportions.”<sup>89</sup>

Government officials have recognized and are responding to the fact that current reporting requirements are insufficient and under-enforced. In 1999, the GAO discovered, to its dismay, that “agencies generally did not

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[hereinafter GAO REPORT ON REPORTING REQUIREMENTS].

<sup>87</sup>Arno & Davis, *supra* note 3, at 691.

<sup>88</sup>*See id.* at 678.

<sup>89</sup>*Id.*

collect or maintain information on licenses granted to third parties by contractors and grantees.”<sup>90</sup> Then, in 2001, the NIH found that “information relating to inventive discoveries and their commercial development is reported neither systematically nor consistently.”<sup>91</sup> The NIH now proposes to address this deficiency by a) requiring contractors to report to the agency the name and trademark of the commercialized invention, b) linking this information to grant data and making this information available on the Internet, c) standardizing and simplifying the reporting requirements, and d) imposing similar requirements on intramural research. These recommendations condemn existing practices as inadequate to protect taxpayers, and, at the same time, embody a promising step in the right direction.

The third taxpayer protection built into Bayh-Dole – the “march-in” provisions – has arguably been even less effective than the reporting requirements. Since the Act was passed in 1980, the march-in provisions have never been exercised and only rarely even been considered. As previously discussed, march-in provisions enable funding agencies to step in when the recipient of a previously-issued exclusive license is not achieving “practical application” of the subject matter invention. “Practical application” means making the subject invention available on “reasonable terms.” There are three other specific conditions that can also trigger the exercise of march-in rights, including whether their exercise is necessary to “alleviate health and safety needs.”<sup>92</sup>

It is clear from both its language and legislative history that the purpose of the march-in provision is twofold. First, it is designed to prevent private entities from sitting on exclusive licenses obtained from the government. For any of a number of reasons – financial, strategic or otherwise – the possibility exists that a private entity might obtain a license to a commercially-viable invention and then fail to act on it. If a

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<sup>90</sup>GAO REPORT ON REPORTING REQUIREMENTS, *supra* note 86, at 15.

<sup>91</sup>NIH RESPONSE, *supra* note 5, at 14.

<sup>92</sup>Bayh-Dole, *supra* note 7, at 37 C.F.R. § 401.14.



significant period of time elapses, the government can “march-in” on the license by issuing another license, exclusive or otherwise, to a separate private entity.

The second purpose of the march-in provision is to prevent corporate windfalls. Inventions subsidized at least in part by taxpayers are, according to the express terms of Bayh-Dole, to be made available on “reasonable terms.” It is well-settled legal doctrine that statutes are, whenever possible, to be accorded their ordinary and plain meaning.<sup>93</sup> The ordinary meaning of “reasonable terms” incorporates reasonable price. This is supported both in parallel circumstances and in the Act’s legislative history.<sup>94</sup> In the context of anti-trust, the United States Court of Appeals for the Sixth Circuit noted that in establishing “reasonable terms,” the setting of “price should be a substantial factor.”<sup>95</sup> Similarly, the United States Court of Appeals for the Fifth Circuit interpreted a statute allowing the Federal Power Commission to establish “reasonable terms” to mean that the “price. . . must be reasonable.”<sup>96</sup> The same result is reached in a number of other situations in which the ordinary meaning of “reasonable terms” was explored, and, it was concluded, deemed to include price.<sup>97</sup>

That the legislators who drafted Bayh-Dole intended to give “reasonable terms” its ordinary meaning is well established in the legislative history. As Arno and Davis have documented, the issue of windfall profits was foremost on the minds of legislators and industry alike. Industry fought to remove the march-in provisions from the final version of the bill. One industry witness testified that march-in rights are a “disincentive” that should be “deleted.”<sup>98</sup> Attempts to water down the meaning of “reasonable terms” failed,<sup>99</sup> as legislators

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<sup>93</sup>Smith v. United States, 508 U.S. 223, 232 (1993); Demarest v. Manspeaker, 498 U.S. 184, 190 (1991).

<sup>94</sup>Commentators Peter Arno and Michael Davis have explored this issue at length. Arno & Davis, *supra* note 3, at 646.

<sup>95</sup>Byers v. Bluff City News Co., 609 F.2d 843, 864 n.58 (6<sup>th</sup> Cir. 1979).

<sup>96</sup>American Liberty Oil Co. v. Federal Power Commission, 301 F.2d 15, 18 (5<sup>th</sup> Cir. 1962).

<sup>97</sup>U.S. v. Mississippi Vocational Rehabilitation for the Blind, 812 F. Supp. 85, 87-89 (S.D. Miss. 1992); U.S. v. United States Gypsum Co., 67 F. Supp. 397, 433-441 (D.D.C. 1946).

<sup>98</sup>Arno & Davis, *supra* note 3, at 661 (testimony of Robert B. Benson, Dir., Patent Department, Allis-Chalmers Corp.).

<sup>99</sup>Peter McCloskey, President of the Electronic Industry Association, suggested that the definition of “practical application” be changed to allow for either “reasonable terms” or “reasonable licensing.” Arno & Davis, *supra* note 3, at 666.

recognized that the march-in provision was the only provision of the bill with teeth to prevent corporate windfalls. At the same time, legislators recognized that march-in rights would be exercised only rarely. Even their infrequent use would be enough to ensure that industry can earn a nice profit but cannot gouge consumers and taxpayers. Infrequent, however, does not mean never.

Since the passage of Bayh-Dole, no funding agency has ever commenced march-in proceedings on its own initiative, though the NIH considered doing so in the case of Taxol. Only once has a third party petitioned the NIH to exercise march-in rights. This petition was primarily concerned with the alleviation of health and safety needs and the timeliness of achieving practical application.<sup>100</sup> In the discussion pertaining to whether the contractee had achieved “practical application” on “reasonable terms,” Dr. Harold Varmus, Director of the NIH, did not expressly consider whether price was a relevant factor.

Believing that the taxpayer protections have failed to live up to their billing, critics argue that Bayh-Dole has enabled the corporate windfalls legislators feared. Government support for health care R&D is considerable – taxpayers spend nearly as much on health care R&D as private industry – and these critics allege that taxpayers could do better on both their intramural and extramural investments.<sup>101</sup> On intramural research, for example, Arno and Davis point out that during the seven-year period from 1993 to 1999, the NIH received royalties totaling only \$200 million – this is less than 1% of the NIH’s funding for intramural research.<sup>102</sup>

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<sup>100</sup>DR. HAROLD VARMUS, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, OFFICE OF THE DIRECTOR, DETERMINATION IN THE CASE OF PETITION OF CELLPRO, INC. (Aug. 1997).

<sup>101</sup>A study conducted at the Massachusetts Institute of Technology, for example, found that of the 21 most important drugs introduced between 1965 and 1992, public funding played a role in 14 (67%). IAIN COCKBURN (UNIVERSITY OF BRITISH COLUMBIA) AND REBECCA HENDERSON (MIT), NATIONAL BUREAU OF ECONOMIC RESEARCH, PUBLIC-PRIVATE INTERACTION AND THE PRODUCTIVITY OF PHARMACEUTICAL RESEARCH (Apr. 1997). *The Boston Globe* reported that 45 of the 50 top-selling drugs from 1992 – 1997 received government funding for some phase of development. Alice Dembner, *Public Handouts Enrich Drug Makers, Scientists*, THE BOSTON GLOBE, Apr. 5, 1998. And perhaps most telling, an NIH report examined the five top-selling drugs in 1995 – Zantac, Zovirax, Capoten, Vasotec and Prozac – and found that taxpayer-funded researchers conducted 55% of the published research projects leading to these drugs’ discovery and development (and foreign academic institutions conducted an additional 30%). NIH OFFICE OF SCIENCE POLICY, NIH CONTRIBUTIONS TO PHARMACEUTICAL DEVELOPMENT: CASE STUDY ANALYSIS OF THE TOP-SELLING DRUGS (Feb. 2000).

<sup>102</sup>Arno & Davis, *supra* note 3, at 640.

Critics also call attention to the high prices charged for pharmaceutical drugs funded partially by taxpayers. One such example is Taxol, a cancer medication. Taxpayers spent \$32 million on the drug's development.<sup>103</sup> Late in its development (during Phase III clinical trials), the drug was transferred to Bristol-Myers Squibb (BMS), for commercialization. BMS' revenues from the drug are now in the neighborhood of \$5 million per day; in 1999, Taxol generated \$1.7 billion in sales for BMS.<sup>104</sup> Generic producers report that Taxol can be manufactured for 7 cents per milligram; Bristol-Myers Squibb is charging \$6.09.<sup>105</sup> Armed with extreme examples such as Taxol, Arno and Davis argue that the "march-in" provisions of Bayh-Dole can be and should be used to force the pharmaceutical industry to charge reasonable prices for drugs.<sup>106</sup>

Representative Bernie Sanders has introduced legislation for a number of years that calls for enforcement of the reasonable pricing clause that already exists in Bayh-Dole.<sup>107</sup> It is strange to think that new legislation is necessary simply to enforce the language of previous legislation, but, in this context, that is apparently what Representative Sanders believes is needed. In 1999, the legislation passed in the House by an overwhelming margin, but it was not pursued in the Senate.<sup>108</sup> In the Senate, Senator Wyden has emerged as an outspoken skeptic of current policy and has placed increasing pressure on the NIH and other government agencies to ensure that taxpayers are being protected.

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<sup>103</sup>DAVID BOLLIER, NEW AMERICA FOUNDATION, PUBLIC ASSETS, PRIVATE PROFITS: RECLAIMING THE AMERICAN COMMONS IN AN AGE OF MARKET ENCLOSURE (2001).

<sup>104</sup>BMS discloses revenues from selected products in its annual 10-K filings with the SEC. These files are available online at <<http://www.edgar.gov>>.

<sup>105</sup>Raquel Pontes de Campos, *supra* note 72.

<sup>106</sup>Arno & Davis, *supra* note 3.

<sup>107</sup>Under the proposed legislation, the Secretary of HHS would have broad discretion to establish criteria and a methodology for determining reasonable prices. The Secretary would, however, be required to consider competitive bidding and certain specific alternatives. The specific competitive bidding methods would award the exclusive license to the firm that charged the lowest price, agreed to the shortest term of exclusivity, or agreed to a reasonable pricing formula after the shortest time or least amount of sales revenue. The secretary could also adopt other methods, and could also set conditions on the license such as required expenditures on research and development. 146 CONG. REC. H4291 (daily ed. June 13, 2000).

<sup>108</sup>*Id.*; See also Robert Pear, *In Policy Change, House Republicans Call for Government Guarantee of Drug Benefits*, N.Y. TIMES, June 14, 2000, at A25.

To summarize, the debate over whether taxpayers are maximizing the return on their investment is a hot one. Everyone agrees that the fundamental goal of tech transfer policy is to maximize human health by commercializing government-funded inventions, and nearly everyone agrees that exclusive licenses are necessary to ensure this commercialization. However, the taxpayer protections built into these exclusive licenses are the subject of fierce debate. Lax enforcement of reporting requirements is widely recognized to be a problem. And, failure to exercise march-in rights has, according to critics, led to corporate windfalls like that demonstrated by Taxol. Going forward, the challenge is to devise a formula for “reasonable terms” that guarantees to private industry neither more than nor less than the financial return necessary to ensure commercialization.

### *II.B.3. Is Technology Transfer Facilitating Research in a Way That Maximizes Human Health?*

The third and final question raised by critics of tech transfer policy steps back to ask a larger question: is technology transfer policy in accord with its broader purpose of maximizing human health and welfare? These critics fear that the current policy may be having the unintended consequence of impeding the progress of biomedical R&D. The critique has two elements. First, critics argue that policy may be encouraging scientists to spend time on profitable medications while discouraging scientists from examining less profitable medications with greater health benefits. Second, critics fear that the profit motive may be impeding scientific progress by stifling the free exchange of information and depleting the public domain of valuable scientific data.

It is widely recognized that universities and university scientists are increasingly driven by a profit motive. Whereas thirty years ago university scientists were most concerned with publishing influential papers and obtaining professional prestige, today, university labs are also driven by patents and profits. Dr. Marc Kirschner, Chair of the Department of Cell Biology at Harvard Medical School, is both excited about and

wary of the fact that scientists are increasingly focused on the application of their scientific ideas outside the lab.<sup>109</sup> “Today,” he states, “every scientist is thinking about starting a company. The expectation is all around to do that.” Universities encourage this by continually asking if the scientists can patent anything that they are doing. And the consequences, according to Kirschner, are troubling. Instead of teaching students, scientists worry about their companies. Instead of collaborating, scientists worry about their property and profit. They are “distracted.”<sup>110</sup> Not only are scientists themselves increasingly concerned with their personal profit, so too are the university laboratories in which they work.

University revenues, whether lump-sum payments or shares of revenue streams, from scientific inventions continue to grow. Yale University, for instance, earned \$151,000 in royalties from its patented inventions in 1982. By 1997, that figure had grown to \$13.5 million.<sup>111</sup> Despite their growth, revenues from royalties still only account for a small percentage of university research budgets. Even the University of California system, which has led universities in tech transfer-related royalty payments in recent years, relies on royalties for only 3% of its total research budget.<sup>112</sup> Yet even these comparatively small revenue streams are tremendously important. In 1998, all but \$2 million of Yale’s \$42 million in royalty revenues came from a single drug – Zerit. The patent on this drug expires in 2008, and “I worry about that everyday,” said Jonathan Soderstrom, director of the school’s Office of Cooperative Research.<sup>113</sup>

The first critique of today’s more profit-driven policy, it is argued, is that it discourages scientists from engaging in research with the greatest potential to maximize human health and welfare. Vaccines, for

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<sup>109</sup>Telephone Interview with Dr. Marc Kirschner, *supra* note 79.

<sup>110</sup>Kirschner also noted that serious conflicts of interest may arise, as when scientists use university property or government grants to specifically further the aims of their companies. He notes, however, that Harvard maintains a strong policy preventing this behavior. *Id.*

<sup>111</sup>M2 COMMUNICATIONS LTD., YALE UNIVERSITY, YALE ANNOUNCES FORMATION OF VALUABLE NEW BIOTECHNOLOGY FIRM (Mar. 27, 1998).

<sup>112</sup>NIH Response, *supra* note 5, at Appendix 2 (Council on Government Relations (COGR) letter to Dr. Wendy Baldwin, Deputy Director, Extramural Research, NIH, June 5, 2001, page 4).

<sup>113</sup>Letitia Stein, *Yale U. Medical School plans uncertain financial future*, THE YALE HERALD, Sept. 24, 1999.

example, have greater potential to maximize human health than once-a-day treatment medications. Ideally, university scientists would focus on the former. Industry, however, has focused on the latter (presumably because it is better for their bottom line.) To the extent that current technology transfer policy has *all* scientists – federal and university scientists included – more focused on profit, the federally-funded scientists may take in the future the same route that industry has taken in the past. Similar logic implies that federally-funded scientists may also decide, as private industry already has, that devoting resources to finding cures for third-world killers like malaria and tuberculosis simply doesn't pay.

Some scientists dispute this logic. Profits, it is argued, tend to correlate with health benefits – after all, people are willing to pay for it. And Kirschner, for one, argues that the problem with malaria lies upstream. “There is enough incentive for scientists,” he argues, “but not enough for drug companies and the NIH.”<sup>114</sup> And the incentive for scientists is not purely prestige – Kirschner claims that the financial incentive is also considerable.

More troublesome to scientists like Kirschner is the second issue with today's profit-driven policy, namely, whether it impedes scientific progress by stifling the free exchange of information. Collaboration and open exchanges of information are critical to scientific progress, and Kirschner has found that the profit motive is stifling collaboration among scientists. Profits depend upon property, leading scientists to keep ideas and progress secret in the hope of keeping discoveries to themselves. Virginia Ashby Sharpe of the Washington, D.C.-based Center for Science in the Public Interest explains that “there are conflicts of interest when an academic researcher's primary commitment to the use of sound procedures in the unbiased search for truth is placed in competition with other [financial or personal] interests that might eclipse the primary commitment.”<sup>115</sup> Along the same lines, Eisenberg argues that patents and property interests can “interfere

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<sup>114</sup>Telephone Interview with Dr. Marc Kirschner, *supra* note 79.

<sup>115</sup>Joseph Paone, *When Big Pharma Courts Academia*, THE SCIENTIST 16[2]:48 (Jan. 21, 2002).

with technology transfer and with the broader goal of promoting continuing technological progress. These goals may sometimes be better served by allocating new knowledge to the public domain.”<sup>116</sup>

A study published in the Journal of the American Medical Association shocked the scientific community by finding that “47% of the academic geneticists who asked other colleagues for information, data and materials related to published research were turned down.”<sup>117</sup> Sheldon Krinsky, a Tufts University researcher who studies the ethics of scientists, notes that “this study shows that commercial interests are beginning to affect the norms of science in a substantial way. Refusing to share scientific information affects one of the most unique aspects of science: its self-correcting function.” Once denied access to the data, the study reports, geneticists were unable to confirm published data, and one in five abandoned a promising line of investigation.

To summarize, a third critical area of debate over technology transfer is whether today’s profit-driven policy may be having the unintended consequence of impeding scientific progress. Current policy may succeed in spawning biotech firms and bringing new medications to the market, but, it may also stifle scientific advance. First, what is most profitable may not necessarily match that which maximizes human health and welfare. Second, the profit motive may be stifling collaboration between scientists and depleting the public domain of information. Addressing these problems may not require wholesale retreat from exclusive licensing, but some tinkering in current policy may be in order.

## **II.C. Perspectives on the Current Debates**

It is, first and foremost, remarkable that there are so few legal voices taking part in these important debates. Taxpayers spend over \$20 billion each year on foundational biomedical research. This investment gives to

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<sup>116</sup>Eisenberg, *supra* note 1, at 1727.

<sup>117</sup>Peter Gerner, *Many scientists won’t share research data, study finds*, CHICAGO TRIBUNE, Jan. 23, 2002, at 10.

the government background rights in a high percentage of biomedical intellectual property. Analyses of this intellectual property that fail to consider the statutory and administrative regime of technology transfer are, in a sense, wholly ignoring the “public” element of this giant public-private partnership. The absence of legal voices is even more alarming if one believes, as previously argued, that property law and the public-private distinction have influenced policy developments.

Second, just as the international implications of tech transfer policy were neglected in the past, so too are they being neglected in these debates of the present. Of course, the international aspects of patent law receive a great deal of attention, particularly those pertaining to the WTO’s agreement on intellectual property (TRIPS). But these debates do not distinguish products funded entirely by private investors from products developed partially with public funding. Inequality is a major source of tension in global politics, and one major component of inequality is unequal access to technology (including life-saving medications). From a foreigner’s perspective, it is bad enough to be denied access to technology because it is in the hands of a private American company. It is even worse if certain rights to this technology are in fact in the hands of the American people. For this reason it is simply shortsighted to develop tech transfer policy without consideration of its impact on international relations.

Interestingly, although international implications have not yet surfaced in the debate over tech transfer, they have begun to surface in other debates concerning the overall mission of health care and access to essential medicines. Representatives from government, private industry, schools of medicine, and schools of public health are increasingly recognizing that current health care policies are giving inadequate attention to the biomedical needs of poorer individuals and nations. Especially since the attacks of September 11<sup>th</sup>, more and



more commentators are coming to view global health care not as a cause of sympathy and charity, but rather as an investment in stability, security and even economic growth.<sup>118</sup> Africa's inability to access HIV/AIDS medications has been the most common subject of this debate. To address these issues, a growing consensus of commentators is advocating "experiments" with new "public-private partnerships."<sup>119</sup> The contours of these partnerships remain for the most part undefined, and completely overlooked is the fact that the drug development process is, in a sense, already a public-private partnership. Thus the successes and failures of tech transfer can inform the development of new public-private partnerships designed to address global inequity, and global inequity, in turn, should inform the development of tech transfer policy.

Third, and finally, all three of the current debates suffer dramatically from a lack of information. The government has, through grossly inadequate enforcement of reporting requirements, lost track of many government-funded inventions. The government has failed to adequately analyze whether any of its inventions are currently or have in the past been languishing in their labs. Universities are failing to abide by the reporting requirements and, it is argued, are also enabling the pursuit of profits to stifle free exchanges of information. Lastly, private industry is contributing to the information blackout by failing to come forward with information about drug development, most notably at the clinical trials phase.<sup>120</sup>

The Transatlantic Consumer Dialogue (TACD) is trying to fill this information vacuum with calls for greater transparency in the field of pharmaceutical economics.<sup>121</sup> Specifically, TACD has recommended that the

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<sup>118</sup>Linda Distlerath, Vice President, Global Health Policy for Merck & Co., Address at the Harvard Health Caucus at Harvard Medical School Spring 2002 Roundtable Series (Feb. 28, 2002); Valerie Epps, Professor, Suffolk University Law School, Address at the Harvard Health Caucus at Harvard Medical School Spring 2002 Roundtable Series (Mar. 20, 2002).

<sup>119</sup>Dr. Lincoln Chen, Director, Global Equity Initiative, Harvard University, Address at the Harvard Health Caucus at Harvard Medical School Spring 2002 Roundtable Series (Feb. 28, 2002). The conceptualization of "new" public-private partnerships has been particularly active in research for an AIDS vaccine.

<sup>120</sup>Congress has the power to subpoena much of this information, but has not exercised its authority to do so.

<sup>121</sup>TRANS ATLANTIC CONSUMER DIALOGUE, TRANSPARENCY OF PHARMACEUTICAL ECONOMICS (2001) (available at

United States and the European Union publish data detailing government outlays on foundational research and clinical testing. TACD also recommends that industry be required to disclose, for any product on the market, costs associated with the product’s development and clinical testing, and how these costs were distributed among the company, government, and third parties.

Good policy cannot be formed in an information vacuum. Yet, that is the location of all three current debates over the direction of tech transfer. The remainder of this article is motivated by a desire to see this vacuum filled. The next section of the article provides a detailed account of the development of one particular drug – Zerit. This fact-based narrative will then be used to inform these current debates.

### III.

#### **Zerit: Technology Transfer in Action**

What follows is a narrative description of the development and commercialization of Zerit, an effective AIDS medication that resulted from successful collaboration among government, universities and private industry. The purpose of telling this factual narrative is to bring a measure of actual, real-world experience to the otherwise untethered debate over technology transfer. This experience can inform the policy-makers grappling with the controversial issues outlined in the previous section. Indeed policy-makers need much more hard information than one could hope to provide in a single article. Nevertheless, some progress may be made.

##### III.A. Why Zerit?

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<[www.tacd.org](http://www.tacd.org)>).

Zerit is the brand name that has been given to the compound d4T. Its generic name is stavudine. It is one of 15 antiretroviral agents now approved to fight AIDS.<sup>122</sup> Effective treatment of HIV/AIDS requires the combined use of several of these medications. Zerit in particular is a nucleoside analogue reverse transcriptase inhibitor (or “nucleoside analog”). As do all nucleoside analogs (like AZT, ddI and ddC), Zerit inhibits the ability of the HIV virus to reproduce.<sup>123</sup>

Zerit is a good candidate for a focused case study of tech transfer for a number of reasons. First, it is an example of technology transfer working at its best. Government funds were dedicated to addressing an emerging health epidemic – HIV/AIDS – and university scientists rushed to the cause. The medication was discovered and then transferred to private industry, who quickly pushed the drug through clinical trials and the FDA approval process. This is the way the process is supposed to work. It is a success story. A critique of current policy should take a look at how it is operating at its best; to instead examine a failure is to set up a straw man. Second, and equally important, the timing of Zerit allows for examination of both its transfer *and* its commercialization under the Bayh-Dole regime. Government grants supporting the foundational research into Zerit occurred in the early 1980s. Under Bayh-Dole, title in the invention vested in Yale University. Then Yale licensed the drug to private industry in 1988, late enough that the Bayh-Dole regime of technology transfer had largely matured. At the same time, the transfer occurred far enough into the past to allow for a record of both its clinical phase and its commercialization. Third, the extent of the

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<sup>122</sup>The antiretroviral agents approved to fight HIV/AIDS fall into one of two general classes: reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs). Within the RTI class are two subclasses - the nucleoside analogue reverse transcriptase inhibitors (nRTIs) and non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) - which are distinguished by their binding site with the HIV reverse transcriptase enzyme. Both subclasses interfere with HIV’s ability to convert viral genetic material, called RNA, into DNA, which the virus needs in order to incorporate into a cell’s DNA. Protease inhibitors act by prohibiting HIV from cleaving large, biologically inactive viral protein precursors (polyproteins) into functionally active viral proteins.

<sup>123</sup>Zerit is known as a relatively “benign” AIDS medication, meaning that its potency is relatively weak compared to other medications on the market. So too, however, are the extent of its side effects, making Zerit a good choice medication for patients who cannot tolerate or do not need the high potency but nasty side effects of more powerful medications. The recommended dosage of Zerit is two capsules (each of 40mg) per day. Nearly all patients remain on the medication for life. However, if all signs of the virus have disappeared then it is possible to stop taking the medication. Should any sign of the virus reemerge, the patient is advised to immediately return to the medication.

AIDS epidemic in Africa raises for Zerot exactly the international issues that have been neglected in past and present debates over the policy's direction.

Fourth, and finally, the extent of the AIDS epidemic has brought attention to the drug's development, shining a light on information that otherwise may not have been available. As the purpose of presenting this narrative is to provide a measure of factual data capable of informing technology transfer policy, the availability of this information is very helpful. Unfortunately, some important information pertaining to Zerot has not yet come to light. Neither Bristol-Myers Squibb nor Yale's Office of Cooperative Research responded to certain research inquiries, leaving some gaps in the narrative. These gaps will be noted as they arise.

### **III.B. An Initial Disclaimer**

The extent of the AIDS epidemic is well-documented and widely publicized. Over 450,000 Americans have died from the disease. In 2002, 323,000 Americans are living with AIDS; 850,000 are living with HIV. There are 40,000 new HIV infections every year.<sup>124</sup> As (nearly) all Americans have access to HIV medication, the rate of death from the disease has, in recent years, tapered off.<sup>125</sup> In other regions of the world, however, the epidemic is far from contained. UNAIDS reports that, in 2001, a staggering 2.3 million Africans died of AIDS. That is more than 6,000 people per day. The same year witnessed the infection of 3.4 million more Africans, bringing the current total of infected individuals on that continent to 28.1 million.

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<sup>124</sup>CENTER FOR DISEASE CONTROL AND PREVENTION, DIVISION OF HIV/AIDS PREVENTION, A GLANCE AT THE HIV EPIDEMIC (2001).

<sup>125</sup>Dr. Frank J. Palella, *Declining Morbidity and Mortality Among Patients With Advanced Human Immunodeficiency Virus Infection*, 338 N.E.J.MED. 853 (Mar. 26, 1998).

Much has been written and much has been read about the emergence and impact of AIDS. It is not the purpose of this article to recount this tragic tale in depth. It is rather my intention to recount the tale of Zerit, and this requires situating its development within the context of the AIDS epidemic. An overview of the epidemic provides necessary background to government, university and private industry action under the Bayh-Dole regime of technology transfer.

“A serious disorder of the immune system that has been known to doctors for less than a year - a disorder that appears to affect primarily male homosexuals - has now afflicted at least 335 people, of whom it has killed 136,” the New York Times reported on May 11, 1982.<sup>126</sup> The article went on to note that “federal health officials are concerned that tens of thousands more homosexual men may be silently affected and therefore vulnerable to potentially grave ailments.... The cause of the disorder is unknown. Researchers call it A.I.D., for acquired immunodeficiency disease, or GRID, for gay-related immunodeficiency.” The disease and news of the disease spread quickly. In February 1983, the New York Times Magazine reported that the disease was “the century’s most virulent epidemic.”<sup>127</sup> By June 1983, 1,450 cases of AIDS had been reported nationwide. More than half of these cases (722) had been diagnosed in New York City, and 262

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<sup>126</sup>Lawrence K. Altman, *New Homosexual Disorder Worries Health Officials*, N.Y. TIMES, May 11, 1982, at C1.

<sup>127</sup>Robin Marantz Henig, *AIDS: A New Disease’s Deadly Odyssey*, N.Y. TIMES, Feb. 6, 1983, at 28.

of these 722 cases had already resulted in death. San Francisco was also hard hit, with an incidence rate 10 times the national average.<sup>128</sup> Although the exact science had not yet been worked out, two “high-risk” groups had been identified: homosexuals and intravenous drug users.<sup>129</sup> By April 1984, over 4,000 Americans had contracted AIDS, most of them homosexuals, and 1,750 of these individuals had died.<sup>130</sup>

In 1984 the U.S. government responded by devoting more public resources to the crisis. In February 1984, legislators debated how best to do this – whether to play a more active role in directing NIH’s attention to the matter, or, allowing for NIH to develop its own response to the emerging epidemic.<sup>131</sup> Ultimately the latter course was pursued, and the NIH began to pay increased attention to AIDS. By mid-1984, more than \$75 million had already been spent on foundational AIDS research, primarily at NIH laboratories in Bethesda, MD.<sup>132</sup> The increase in funding had begun to produce results. In April 1984, at the NIH lab in Bethesda, Dr. Gallo confirmed his recent study identifying the family of viruses central to AIDS. Gallo also developed a cell line that made it possible to grow the viruses, an event that was hailed at the time as “a turning point” in the fight against AIDS.<sup>133</sup> Meanwhile, a team of French researchers working in Paris succeeded in singling out from the family Gallo had identified the particular strain of the virus known as HIV.<sup>134</sup>

The period from 1984 to 1986 witnessed the unfolding of three important strands of the AIDS crisis. First, the two high-risk groups – homosexuals and intravenous drug users – continued to receive the lion’s share of attention, and with this attention came a certain measure of ostracization. The public was under-informed

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<sup>128</sup>Sam Roberts, *Medical Detectives Hunt Clues to AIDS Outbreak*, N.Y. TIMES, June 4, 1983, at 25.

<sup>129</sup>*Id.*

<sup>130</sup>Philip M. Boffey, *A Likely AIDS Cause, But Still No Cure*, N.Y. TIMES, Apr. 29, 1984, at 22.

<sup>131</sup>Robert Pear, *Congress Rethinks Its Hands-Off Policy on Medical Research*, N.Y. TIMES, Feb. 26, 1984, at 3.

<sup>132</sup>President Reagan budgeted \$54 million for fiscal year 1985. Boffey, *supra* note 130.

<sup>133</sup>*Id.*

<sup>134</sup>Initial findings were reported as early as May 1983, but the findings were confirmed in April 1984. *Id.*

as to how the virus was transmitted, causing many to shun interaction with members of the high-risk groups. These two groups were thus hard hit not only by the disease itself, but also by the ostracization that came with it. Of course, members of these groups were not the *only* individuals coming down with the virus. Others were also inflicted first by the virus, and then by the ostracization that came with it. In New York, for example, children who contracted the disease were not allowed to return to school.<sup>135</sup>

Second, by the end of 1986 it had become quite clear that AIDS was an epidemic of not national but *international* significance. According to the World Health Organization (WHO), it had become “a health disaster of pandemic proportions.”<sup>136</sup> In October 1986, the WHO reported that from January through mid-September, the number of AIDS cases recorded worldwide had risen from 20,476 to 31,646.<sup>137</sup> While the vast majority of these cases were recorded in the United States, the WHO also reported sharp increases in West Germany, France, Italy, Australia and New Zealand. The most striking increase was in Africa, where 10 countries reported 1,003 cases by mid-September, up from 31 reported at the start of the year. By December, the New York Times was reporting that Latin America and Asia were also facing potential AIDS crises. The WHO reported that Brazil was facing an “African-style epidemic of AIDS.”<sup>138</sup> No medications had yet made it to the market, and precious few AIDS patients were living longer than five years.

Third, the scientific community continued, unsuccessfully, their frustrating struggle to find a cure.<sup>139</sup> Although the government stepped up its funding – for fiscal year 1986, Congress appropriated \$244 million to fight AIDS – \$140 million dedicated to scientific research and the remainder going to prevention and education<sup>140</sup> – little progress had been made. “Vast ignorance” remained, and scientists did not believe that

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<sup>135</sup>Dudley Clendinen, *Schools in New York Will Admit an AIDS Pupil But Not 3 Others*, N.Y. TIMES, Sept. 8, 1985, at 1.

<sup>136</sup>Lawrence K. Altman, *Global Program Aims to Combat AIDS ‘Disaster,’* N.Y. TIMES, Nov. 21, 1986, at 1.

<sup>137</sup>Thomas W. Netter, *AIDS Cases Are Said to Rise Sharply Worldwide*, N.Y. TIMES, Oct. 5, 1986, at 1; *See also* Ed Hooper, *An African Village Staggers Under the Assault of AIDS*, N.Y. TIMES, September 30, 1986, at C1.

<sup>138</sup>*AIDS in the Third World*, N.Y. TIMES, Dec. 9, 1986, at C15.

<sup>139</sup>Lawrence K. Altman, *The Doctor’s World: Search for an AIDS drug is case history in frustration*, N.Y. TIMES, July 30, 1985, at C1.

<sup>140</sup>Morton Hunt, *Teaming Up Against AIDS*, N.Y. TIMES, Mar. 2, 1986, at 42.

the disease could be defeated within a few years.<sup>141</sup> On the positive side, several promising leads had been identified, though none of these leads had emerged from the laborious process of clinical testing mandated by the FDA. It was around this time – the end of 1986 – that Dr. William Prusoff and Dr. Tai-Shun Lin discovered that d4T, the compound that would come to be marketed under the brand name of Zerit, was active against the HIV virus.

### *III.C.2. The Preclinical Phase*

Among the many scientists who responded to the emerging AIDS epidemic were two professors at Yale University – Dr. Tai-Shun Lin and Dr. William Prusoff. These scientists had years of experience exploring novel antivirals. Early efforts had produced idoxuridine, a clinically-useful, FDA-approved antiviral agent. In the early-1980s, the scientists had been focusing their attention on several families of compounds with potential activity as antivirals; in 1984, Dr. Prusoff and Dr. Lin reported to the NIH that 5'-amino nucleoside analogs had “good potential as antivirals” and that 3'-amino nucleosides had “good anti-cancer activity.”<sup>142</sup> The scientists continued to receive NIH funding for their efforts, and they now began to test these compounds for activity as antivirals. The jewel among these compounds would turn out to be d4T (3'-deoxythymidin-2'-ene), a compound first synthesized in 1966, by Dr. Jerome P. Horowitz, at the Michigan Cancer Foundation (Karmanos Cancer Institute).<sup>143</sup>

When Dr. Horowitz first synthesized d4T, he had been working with federal funding provided by the National Cancer Institute.<sup>144</sup> Federal funding was also the primary means of support for the research later

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<sup>141</sup>Erik Eckholm, *AIDS: Scientists voice concern over research*, N.Y. TIMES, Nov. 4, 1986, at C1.

<sup>142</sup>DR. WILLIAM PRUSOFF, IODODEOXYURIDINE, IODO-DNA AND BIOLOGICAL ACTIVITY, GRANT APPLICATION TO THE NIH, 2R01CA005262-25 (1985).

<sup>143</sup>The compound is more fully described as 3'-deoxy-2', 3 -didehydrothymidine.

<sup>144</sup>Tina Rosenberg, *How to Solve the World's AIDS Crisis*, N.Y. TIMES MAGAZINE, Jan. 28, 2001, at 31.



conducted at Yale University – Dr. Prusoff had been working with NIH grants for decades.<sup>145</sup> Importantly, the NIH funding was supplemented by sizeable financial support from private industry. In the early 1980s, Bristol-Myers gave \$500,000 to Yale University to help finance research in antivirals.<sup>146</sup> In return, Bristol-Myers was given the right of first refusal to license any Yale inventions in this field. Importantly, according to Dr. Prusoff, Bristol-Myers’ grant did not enable the company to direct the course of Yale’s research. University scientists maintained “complete academic freedom.”<sup>147</sup> At the same time, despite their academic freedom, the university scientists were nevertheless able to take advantage of the resources that Bristol-Myers laboratories had to offer.

The events that follow show an extraordinary level of cooperation among the NIH, universities and Bristol-Myers. In 1985, Dr. Prusoff and Dr. Lin synthesized the d4T compound. The scientists sent it to Bristol-Myers to test for retroviral activity, though not for activity against the AIDS retrovirus in particular. Bristol-Myers reported that d4T was, in fact, active against retrovirus. The next step involved testing the compound for activity against the AIDS retrovirus in particular, but neither Yale nor Bristol-Myers had the laboratory capacity to do so. (Remember that the HIV virus had itself been identified less than two years prior.) Thus, in January 1986, Bristol-Myers sent d4T to the NIH to test for activity against AIDS. Despite the increase in government resources being devoted to AIDS, the NIH was swamped and therefore slow to conduct the test. The end of the summer arrived and there was still no word from the NIH. In September 1986, rather than continuing to wait on the NIH, Dr. Prusoff decided to send the compound to his friend and colleague, Dr. Raymond Schinazi, at Emory University. The Emory laboratory had the necessary technology to test the compound for activity against AIDS. Within the month Dr. Schinazi reported back to

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<sup>145</sup>The specific grant that funded the research into d4T ran from 1981 through 1985. DR. WILLIAM PRUSOFF, SYNTHESIS AND BIOLOGICAL EVALUATION OF A NOVEL SERIES OF NUCLEOSIDE ANALOGS, GRANT APPLICATION TO THE NIH, 1P01CA028852-010001 (1981). Another NIH grant supporting the work of Dr. Prusoff at this time was a longstanding study that ran from 1971 through 1994. DR. WILLIAM PRUSOFF, *supra* note 142.

<sup>146</sup>Interview with Dr. William Prusoff, *supra* note 79.

<sup>147</sup>*Id.*

Dr. Prusoff that d4T was in fact active against AIDS.<sup>148</sup> NIH delivered the same positive news two months later, in November 1986. On December 17, 1986, Yale filed for a patent.<sup>149</sup> In accordance with the reporting procedures mandated by Bayh-Dole, the patent application recognized that federal funds contributed to the compound's development.<sup>150</sup> Results of the research were submitted for publishing in 1987 and ultimately published in 1988.<sup>151</sup>

The initial laboratory collaboration was successful: Government funds were allocated to respond to an emerging health epidemic; experienced university scientists took advantage of this federal funding and quickly turned their attention to the field; and private industry saw an opportunity and contributed both financial and technical support. Interestingly, while foundational research is typically regarded as the work of government and universities, in the case of Zerit, private industry joined in the collaboration to speed the process along. Dr. Prusoff indicated that without the financial and technical assistance of Bristol-Myers, the same result would have likely been obtained, but the process would have taken much longer. At the same time, neither Bristol-Myers nor Yale had all of the necessary expertise and technical capacity. When they reached an impasse, they called first on the NIH and then on Emory University to conduct the necessary testing.

### *III.C.3. From Clinical Testing to FDA Approval*

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<sup>148</sup> *Id.*

<sup>149</sup> The United States patent was ultimately granted on Dec. 18, 1990 (Patent # 4,978,655). The patent expires on June 25, 2008. Yale has also been granted patent rights in Austria, Belgium, Canada, France, Germany, Greece, Italy, Japan, Korea, Liechtenstein, Luxembourg, Netherlands, Philippines, Spain, Sweden, Switzerland, and the United Kingdom. Yale filed for patent rights in Australia, Denmark, Egypt, Finland, Hong Kong, Ireland, Israel, Mexico, New Zealand, Portugal, Romania, Singapore, South Africa, and Taiwan.

<sup>150</sup> The patent states that "This invention was made with United States government support under Grant CA-28852 from the NIH. The United States Government has certain rights in this invention." (Patent # 4,978,655).

<sup>151</sup> TS Lin TS, WH Prusoff, and RF Schinazi, *Potent and selective in vitro activity of 3'-deoxythymidin-2'-ene (3'-deoxy-2',3'-didehydrothymidine) against human immunodeficiency virus*, BIOCHEM PHARMACOL. 36(17):2713-8 (Sep. 1987).

Dr. William Prusoff, Biochem. Pharmacol. 33: 4419-4422 (1988). In the same year, similar results were published by one team of Japanese scientists and another team of European scientists. Credit for first discovering the compound's activity, however, was ultimately bestowed upon the team operating at Yale.

Having established that the compound was active against the AIDS retrovirus, scientists then turned to the laborious and time-consuming process of conducting clinical trials. The FDA reports that out of 100 drugs beginning the human clinical testing process, 20 are ultimately approved for marketing.<sup>152</sup> Because of the expense of conducting these trials, the government and universities typically seek at this stage commitment from private industry. The government does not take a medication through the clinical trials process entirely on its own.<sup>153</sup> Zerit was no exception to this rule. Yale contacted Bristol-Myers (who, as previously mentioned, had obtained the right of first refusal by way of a prior grant) to discuss terms for licensing.<sup>154</sup> On January 12, 1988, the two parties signed an agreement under which Bristol-Myers obtained an exclusive license to market and distribute d4T.<sup>155</sup> (The following year, in October 1989, Bristol-Myers merged with Squibb to create what was, at that time, the second largest pharmaceutical company in the world.)

As previously mentioned, clinical trials are predominantly funded by the private sector. However, public and university participation can often play an important supporting role.<sup>156</sup> First, trials are often conducted at university laboratories, and the universities themselves provide certain costs (including laboratory space, salaries of participating doctors, etc.). Second, private industry will at times desire independent, objective scientists to conduct a clinical trial, for such trials are looked upon favorably by the FDA in the approval process. These independent trials are funded primarily by the government and by institutes for research. Third, where there is a pressing public health need, the government may take certain measures to speed

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<sup>152</sup>U.S. FOOD AND DRUG ADMINISTRATION & CENTER FOR DRUG EVALUATION AND RESEARCH, SPECIAL REPORT, THIRD EDITION, FROM TEST TUBE TO PATIENT: IMPROVING HEALTH THROUGH HUMAN DRUGS (1999) (available at <[www.fda.gov/cder/about/whatwedo/testtube-3a.pdf](http://www.fda.gov/cder/about/whatwedo/testtube-3a.pdf)>). This statistic is corroborated by PhRMA.

<sup>153</sup>Telephone Interview with Dr. Henry Sacks, Mount Sinai Medical Center, Clinical Testing (Mar. 20, 2002).

<sup>154</sup>The author was unable to obtain more detailed information on the process by which Bristol-Myers negotiated for this exclusive license. It is thus unknown whether Bristol-Myers was eager to pursue their right of first refusal, or, whether Yale had to push hard to find a corporation willing to undertake the clinical trials.

<sup>155</sup>James Love (visited Mar. 22, 2002) <<http://www.cptech.org/ip/health/aids/gov-role.html>>.

<sup>156</sup>Telephone Interview with Henry Sacks, *supra* note 153.

drugs through the clinical testing and FDA-approval process. As AIDS was a pressing public health need, the government did in fact assist d4T in the clinical testing and approval process.

From 1988 through 2001, there were 109 clinical trials involving d4T – 53 sponsored by the government and 59 sponsored by private industry (predominantly by Bristol-Myers Squibb (BMS)).<sup>157</sup> Of these, six trials supported d4T's application for FDA approval: three Phase I studies, one Phase II study, one Phase III study, and one "investigational use" study. Phase I human clinical testing establishes safe dosage levels. The first of three Phase I tests on Zerit began on March 23, 1989.<sup>158</sup> This test, which succeeded in establishing a maximum tolerated dose, was conducted at the Brown University AIDS program and had an accrual of 41 patients. The second Phase I test was conducted at the Division of Infectious Diseases at Cornell University Medical College, and it also had an accrual of 41 patients.<sup>159</sup> This test succeeded in establishing safe dosage. The third Phase I study was a pharmacology study involving 23 patients.<sup>160</sup> These Phase I trials were jointly supported by BMS, universities and grants from the NIAID of the NIH.<sup>161</sup> The Phase II trial, conducted at the University of Arizona, Tucson, established the safety of administering oral dosages of d4T three times per day.<sup>162</sup> This test, involving 152 patients, was also supported by both BMS and the government.<sup>163</sup>

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<sup>157</sup> *ACTIS Database* (visited Mar. 22, 2002) <www.actis.gov>. The majority of these tests were conducted after the drug had already obtained FDA approval. Such testing is generally conducted on potential additional uses and applications of the drug.

<sup>158</sup> MJ Browne, KH Mayer, SB Chafee, MN Dudley, MR Posner, SM Steinberg, KK Graham, SM Geletko, SH Zinner, SL Denman, et al., *2',3'-didehydro-3'-deoxythymidine (d4T) in patients with AIDS or AIDS-related complex: a phase I trial*, 167 J. Infect. Dis. 21 (1993). See also G. Skowron, *Overview of Phase I & Phase II*, 171 J. Infect. Dis. (Supp2), S113 (1995).

<sup>159</sup> HW Murray, KE Squires, W Weiss, S Sledz, HS Sacks, J Hassett, A Cross, RE Anderson, LM Dunkle, *Stavudine in patients with AIDS and AIDS-related complex: AIDS clinical trials group 089*, 171 J. Infect. Dis. (Supp.2), S123 (1995).

<sup>160</sup> MN Dudley, KK Graham, S Kaul, S Geletko, L Dunkle, M Browne, K Mayer, *Pharmacokinetics of Patients with AIDS*, 166 J. Infect. Dis. 480 (1992).

<sup>161</sup> NIH grants supporting the clinical testing of d4T include Grant #s 5M01RR000071-270199, M01RR000071-290246, and 5M01RR000071-300246.

<sup>162</sup> EA Petersen, CH Ramirez-Ronda, WD Hardy, R Schwartz, HS Sacks, S Follansbee, DM Peterson, A Cross, RE Anderson, LM Dunkle, *Dose-related activity of stavudine in patients infected with human immunodeficiency virus*, 171 J. Infect. Dis. (Supp. 2) S131 (1995).

<sup>163</sup> NIH grants supporting this clinical test included Grant #s 5M01RR000071-290260, 5M01RR000071-300260, and 5M01RR000071-310260.

The year was 1992, a time during which each AIDS drug in the pipeline, including Zerit, was the subject of great hope and anticipation. AZT had been approved by the FDA in 1987, ddI in 1991, and ddC in 1992, yet these three medications had not completely met the AIDS community's need for effective medications. There was thus pressure on the government to speed promising AIDS drugs through the clinical trial and approval process.<sup>164</sup> Indeed since mid-1985, at which time 6,000 Americans had already died from AIDS, the FDA had been pressured to relax its otherwise stringent clinical testing requirements for AIDS medications.<sup>165</sup> Participants in clinical trials had a 50-50 chance of receiving a mere placebo, and the half that received the active drug risked dangerously strong side effects. At the end of 1986, of 17,000 AIDS patients in the U.S., 4,000 were participating in drug trials. These patients "considered themselves lucky."<sup>166</sup> In 1990, the National Commission on AIDS focused specifically on enrollment in clinical studies and reported to President Bush that the government's effort at drug development "falls far short of the mark." The Commission found that only 12,000 people were involved in clinical trials, a "pitifully small" figure compared to the number eligible.<sup>167</sup>

By 1992, just three years after its first Phase I clinical trial began, d4T had successfully emerged from both Phase I and Phase II trials and was making waves in the AIDS community. Doctors at AIDS clinics in hard-hit areas – New York and San Francisco – had been following the drug's progress ever since its first Phase I trial.<sup>168</sup> Now that stavudine had been found to be safe and initial data on its effectiveness were positive, the number of AIDS patients clamoring to get their hands on it was considerable.<sup>169</sup>

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<sup>164</sup>Gina Kolata, *Interest Grows in Licensing Shortcut for Two AIDS Drugs*, N.Y. TIMES, Sept. 25, 1990, at 3.

<sup>165</sup>Harry Schwartz, *Finding a Cure for AIDS*, N.Y. TIMES, Aug. 22, 1985, at 23.

<sup>166</sup>Erik Eckholm, *Should the Rules be Bent in an Epidemic?*, N.Y. TIMES, July 13, 1986, at 30.

<sup>167</sup>Philip J. Hiltz, *Panel Issues Broad Attack on U.S. Response to AIDS*, N.Y. TIMES, Aug. 22, 1990, at 4.

<sup>168</sup>Interview with Dr. Kevin Williams, in Cambridge, Mass. (Nov. 6, 2001).

<sup>169</sup>*Id.*

In May 1992, BMS began a Phase III trial involving 822 patients.<sup>170</sup> Compared to the Phase I and Phase II studies, the Phase III study relied more heavily on funding from BMS (though it was coordinated at the Health Sciences AIDS Center at the University of Utah School of Medicine). It was also, in part, supported by government funding.<sup>171</sup> Because stavudine was such a promising essential medicine, thousands of patients desired access to the drug – many more than the 822 participating in the study. In October 1992 the FDA responded to this demand by making d4T the first medication ever to receive from the FDA so-called “parallel-track” status for expanded “investigational use.” This new program was developed by the FDA to allow for wider access to promising medications in late stages of clinical testing. BMS coordinated the study and provided the medication for free, while doctors in medical centers and clinics around the country monitored its effects on participating patients. In less than eight months, over 8,000 patients obtained access to the medication through this trial.<sup>172</sup>

On December 28, 1993, BMS filed a New Drug Application (NDA) with the FDA. Under the FDA’s accelerated approval policy for essential medications, clinical testing must demonstrate that the compound has an effect on a surrogate endpoint and that the compound satisfies an unmet medical need. For d4T, this surrogate endpoint was increased CD4 cell counts (cells that the human body uses to fight HIV). The Phase III trial obtained this surrogate endpoint in 359 patients,<sup>173</sup> and d4T was approved by the FDA on June 24, 1994.<sup>174</sup> By this date, more than 13,000 patients had obtained access to d4T through the “investigational

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<sup>170</sup>SL Spruance, AT Pavia, JW Mellors, R Murphy, J Gathe Jr., E Stool, JG Jemsek, P Dellamonica, A Cross, L Dunkle, *Clinical efficacy of monotherapy with stavudine compared with zidovudine in HIV-infected, zidovudine-experienced patients. A randomized, double-blind, controlled trial, Bristol-Myers Squibb Stavudine/019 Study Group*, 126(5) *Ann Intern Med* 355 (Mar. 1997) (Trial # AI455-019).

<sup>171</sup>NIH grants supporting this clinical test included Grant #s 5M01RR000071-300287, 5M01RR000071-310287, 5M01RR000071-320287, and 2M01RR000071-330287.

<sup>172</sup>RE Anderson, LM Dunkle, L Smaldone, M Adler, C Wirtz, D Kriesel, A Cross, RR Martin, *Design and implementation of the stavudine parallel-track program*, 171 *J Infect Dis* (Suppl 2) S118 (Mar. 1995).

<sup>173</sup>John Schwartz, *FDA Clears 4th Drug to Fight AIDS*, WASHINGTON POST, June 28, 1994, at A12. In clinical trials of 359 AIDS patients whose immunity-boosting CD4 cells had dropped to a median level of 250 cells per cubic millimeter of blood, the drug was found to increase the count by 24 cells per cubic millimeter of blood. Patients taking AZT showed a decline of 22 cells over a 12-week treatment period.

<sup>174</sup>*Id.*

use” program.<sup>175</sup> Initial shipments of the drug to wholesalers began on July 8, 1994 at the price of \$6.22 per day, making Zerit the first new anti-HIV drug to reach the market in nearly two years.<sup>176</sup> Overall, Zerit was the fourth AIDS medication to reach the market, the first three being zidovudine (AZT), didanosine (ddI) and zalcitabine (ddC). (ddI had been marketed by BMS under the brand name Videx since October 1991.) Further clinical testing on the final endpoint continued through mid-1995.<sup>177</sup>

Only five years had passed since the first Phase I trial had begun, and Zerit had already been used by 13,000 patients and was on the market for widespread use. BMS and the FDA were congratulated for speeding up a process that generally takes *much* longer than five years. Indeed antiretrovirals (such as Zerit) have the shortest time-to-approval of any class of drugs beginning clinical testing: the mean is 44.6 months, which is half the industry average of 87.4 months.<sup>178</sup> According to Dr. Henry Sacks, a member of the NIH-supported AIDS Clinical Research team and a leading researcher on several d4T clinical trials, the participation of BMS was absolutely essential in the clinical testing of Zerit. At the same time, the government’s financial support and the FDA’s policies of “investigational use” and expedited approval helped to speed the process along. Thus, interestingly, the story of Zerit indicates that what is typically conceptualized as a clean division of labor (with the government doing the preclinical phase and private industry doing the clinical phase) is not quite so clean. BMS support helped to speed the development process along in its initial, foundational stages, and the government’s support speeded the process along in its later stages.

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<sup>175</sup>CW Henderson, *Company Announces FDA Approval for HIV Drug*, AIDS WEEKLY, July 11, 1994.

<sup>176</sup>*Id.*

<sup>177</sup>John Schwartz, *FDA Sees Promise in New Anti-AIDS Drugs; Commissioner Indicates Agency Will Move Swiftly to Approve 'Protease Inhibitors' for Market*, WASHINGTON POST, Nov. 6, 1995, at A4. BMS ultimately obtained full marketing approval from the FDA in 1996. *Bristol-Myers Drug Approved*, WALL STREET JOURNAL, Jan. 5, 1996, at B10.

<sup>178</sup>K Kaitin & E Healy, *The new drug approvals of 1996, 1997, and 1998: drug development trends in the user fee era*, 34 DRUG INFORMATION JOURNAL 1-14 (2000).

Estimates of BMS' out-of-pocket expenses on the development of Zerit are in the \$10 million to \$40 million range.<sup>179</sup> According to the Tufts Center, the average cost of clinical trials for approved drugs is about \$25 million (in 1995 dollars). Considering the fact that the clinical trials for Zerit took half as long as usual and received above average levels of government funding, it is probable that BMS' out-of-pocket expenditures on clinical trials were less than \$25 million.<sup>180</sup> BMS' out-of-pocket expenditures also include its initial grant to Yale University of \$500,000, and, more significantly, the cost of regulatory filings (which is well into the millions). After adjusting these figures for both risk and opportunity cost of capital, the overall cost to BMS likely falls in the \$150 million to \$300 million range (in 1995 dollars).<sup>181</sup> Considering the relatively high level of taxpayer support for Zerit's development and the speed with which it passed through clinical trials and FDA approval, this range is consistent with the OTA's 1993 report pegging the average cost of developing a drug at \$500 million.

#### *III.C.4. Zerit Hits the Market*

As might be expected from a drug that had 13,000 people volunteer for clinical testing, the market received Zerit, the fourth HIV/AIDS medication to obtain FDA approval, with open arms. Initial shipments in 1994 were sold to wholesalers at the price of \$6.22 per day. In 2002, the retail cost of the medication hovers in the \$9 per day range (or \$3,300 per patient per year). BMS' revenues from sales of Zerit had, by December

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<sup>179</sup>Interview with Dr. William Prusoff, *supra* note 79.

<sup>180</sup>Zerit's clinical trials were also likely cheaper than the average because the Phase III study involved relatively fewer patients. This was made possible by the fact that thousands more patients were able to access the drug, at little cost to BMS, through the "parallel track" program.

<sup>181</sup>Assume for purposes of this calculation that the clinical trials on Zerit were of average cost. According to the Tufts Center, the average expenditure on clinical trials is \$25 million (in 1995 dollars). To adjust for the risk involved with unsuccessful trials, the Tufts Center increases this figure to \$55 million. Add \$25 million for regulatory filings (which is on the high end) and then double or triple the figure to adjust for opportunity cost of capital (the Tufts Center doubles it), and you end up with a cost of roughly \$150 to \$300 million.



31, 2000, exceeded \$2.3 billion.<sup>182</sup>

For AIDS patients with prescription-drug coverage, the cost of the medication is borne by insurance companies. (The cost is then, presumably, passed through to citizens and employers in the form of higher premiums.) There are, however, many Americans who do not possess prescription drug coverage (such as those on Medicare) and who are unable to pay for Zerit out of pocket. The government's AIDS Drug Assistance Program (ADAP) covers many of these individuals. But there are still some patients who qualify for neither ADAP nor Medicaid (which offers prescription drug coverage). Thus, there are some patients who are unable to afford the medication and are unable to get their hands on it.<sup>183</sup>

As set forth in the licensing agreement between BMS and Yale, Yale receives royalties from sales of Zerit. Of these revenues, 70% go to the university and 30% go to the drug's two founders – Dr. Prusoff and Dr. Lin. In 1999, Yale's portion of the royalties was \$40 million, which was 95% of the university's total revenues from royalties on its patents (\$42 million). On October 5, 2001, Yale exchanged its rights to Zerit's revenues for an up-front payment of \$115 million. About \$60 million of this total is going into a new medical complex.<sup>184</sup> Yale is among the first universities to have completed a so-called monetizing deal on its patent royalties.

### *III.C.5. The Rich Have, the Poor Have Not*

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<sup>182</sup>In 1996, BMS' revenues were \$140 million; in 1997, \$398 million; in 1998, \$551 million; in 1999, \$605 million; and, in 2000, \$618 million. BMS discloses revenues from selected products in its annual 10-K filings with the SEC. These files are available online at <<http://www.edgar.gov>>.

<sup>183</sup>Interview with Dr. Kevin Williams, *supra* note 168.

<sup>184</sup>The terms of this complicated deal are explained in Goldie Blumenstyk, *Turning Patent Royalties Into a Sure Thing*, THE CHRONICLE OF HIGHER EDUCATION, Oct. 5, 2001, at 26.

The final piece of Zerit’s narrative is the growing AIDS epidemic in poorer nations, and the pressure that this epidemic has placed on those with rights to Zerit to allow for greater access. The combination of effective medications and strong prevention programs have, to a large extent, contained the spread and morbidity of AIDS in the United States. But the same cannot be said of the containment of HIV/AIDS in other parts of the world, and particularly in Africa. As previously mentioned, UNAIDS reported that a staggering 2.3 million Africans died of AIDS in 2001 and that a further 28.1 million Africans are infected with the virus. In 2000, between 10,000 and 25,000 Africans – fewer than 0.1 percent of those with HIV/AIDS – were being treated with antiretroviral medicines.<sup>185</sup> Harvard economist Jeffrey Sachs, Chair of the World Health Organization (WHO) Advisory Commission on Macroeconomics and Health, said that “it’s as though the Black Death were going on in Europe in the 14th century, and China were sitting on a cure and saying, ‘Why should we help?’ We would consider it the crime of the millennium if that had happened, and yet we seem to be able to accommodate this without much trouble.”<sup>186</sup> More specifically, what we are “accommodating” is the fact that for many years, even in the face of this awesome epidemic, neither pharmaceutical companies nor Yale University nor the U.S. government – the three parties that developed Zerit and that possess rights to Zerit – acted to make Zerit available to African nations at discounted prices.

The enormity of Africa’s AIDS epidemic was recognized in the early 1990s, while Zerit was still undergoing Phase I and Phase II clinical tests.<sup>187</sup> In 1991, the WHO organized a meeting attended by high-level representatives from 18 large pharmaceutical companies, including BMS. The purpose of the meeting was to ensure that AIDS medications, once developed and approved, would be made available at a cost that all

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<sup>185</sup>Bill Brubaker, *The Limits of \$100 Million; Epidemic’s Complexities Curb Impact of Bristol-Myers’s Initiative*, WASHINGTON POST, Dec. 29, 2000, at A1.

<sup>186</sup>Barton Gellman, *An Unequal Calculus of Life and Death; As Millions Perished in Pandemic, Firms Debated Access to Drugs; Players in the Debate Over Drug Availability and Pricing*, WASHINGTON POST, Dec. 27, 2000, at A1.

<sup>187</sup>One article reported that at least 10,000 Ugandans had developed AIDS (mainly through heterosexual contact) and nearly 800,000 of the nation’s roughly 17 million citizens were believed to be infected with the virus. Kathleen Hunt, *Scenes From a Nightmare*, N.Y. TIMES, Aug. 12, 1990, at 25.

countries could afford. Director General Hiroshi Nakajima opened the talks by noting that “By the end of this decade, there will have been a cumulative total of... 40 million HIV infections – I repeat, 40 million – in men, women and children. Over 90 percent of these will be in developing countries.”<sup>188</sup> But the companies felt threatened by WHO’s plans to make medications available at low prices. At that time, BMS was about to receive FDA approval for its first AIDS medication, ddI. Rather than work alongside the WHO to develop a plan to make this medication available to African nations at low prices, BMS Senior Vice President Stephen Carter downplayed the impact that AIDS might have on the continent relative to other health concerns.<sup>189</sup> WHO’s negotiations with private industry made little headway for many years.

Throughout the 1990s, the price of AIDS medications in Africa remained high. Zerit was sold by BMS for roughly the same price in Africa as in the United States – \$3,300 per patient per year. According to generic producers, the cost of its manufacture and distribution is only \$300 per year.<sup>190</sup> Why was BMS so reluctant to act on its own initiative to make the medication available at a lower price?

One explanation might be that BMS wanted to earn profits on sales of Zerit in Africa. This explanation, however, does not withstand scrutiny. The entire continent of Africa accounts for only 1% of worldwide sales of pharmaceutical medications. In 1998, it accounted for only 0.03% of BMS’ HIV/AIDS drug sales.<sup>191</sup> Certainly BMS was not counting on earning significant profit from Zerit in Africa, and in 1998, James Sapirstein, BMS sales executive in charge of HIV/AIDS global sales, indicated as much: “South Africa was not a priority. The thinking [was] that we should just write the business off, that it was impossible, that there was no money to be made” in Africa.<sup>192</sup>

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<sup>188</sup>Barton Gellman, *supra* note 186.

<sup>189</sup>*Id.*

<sup>190</sup>Raquel Pontes de Campos, *supra* note 72.

<sup>191</sup>Bill Brubaker, *supra* note 185.

<sup>192</sup>*Id.*

Another explanation might be that lower prices could not solve the AIDS epidemic. This explanation, however, also fails to withstand scrutiny. If BMS had offered to sell Zerit at cost, Zerit would have still failed to reach the vast majority of Africans with AIDS – many African nations spend less than \$2 per person per year on health care. Huge amounts of foreign aid were and continue to be needed, and this aid is spent primarily on health care infrastructure, education and prevention programs.<sup>193</sup> These expenditures, it is argued, are a more effective way to allocate the available funds.<sup>194</sup> This may indeed be true, but it is equally true that lower drug prices would have left more money in the pot to spend on prevention programs or to purchase more drugs. Lower prices may not have alone contained the epidemic, but they would have saved lives.

Rather, the true reason why BMS did not lower its price for Zerit in South Africa was voiced by Michael Scholtz, a German national who began work for the WHO after 21 years as a manager at Ciba-Geigy and SmithKline Beecham. Scholtz said that “if cheaper drugs in Africa put downward pressure on the global price, then the core markets of the pharmaceutical industry are at risk.”<sup>195</sup> The problem, in other words, was the fear that drugs made available at low prices in Africa would find their way back into the markets of richer nations. This would undermine the profits that the pharmaceutical industry earns at home. Absent adequate assurances that Zerit would not be re-exported back to the United States, BMS refused to flood the continent with its medication. This is the problem of so-called “parallel imports,” and it affects not only pharmaceutical drugs but also music, videos, jeans, cars and countless other consumer products.

African nations, meanwhile, desperately needed large quantities of HIV/AIDS medications. Zerit was not

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<sup>193</sup>It is widely recognized that significantly more money is necessary to address the AIDS crisis in Africa, and that this money will simply have to come, if at all, from wealthy nations and citizens. “The brutal fact,” health economist William McGreevey told an invitation-only World Bank audience on May 22, 1998, was that “those who could pay” for Africa’s AIDS therapy “are very unlikely to be persuaded to do so.” Barton Gellman, *supra* note 186.

<sup>194</sup>In 1997, Jonathan Quick of WHO’s essential medicines program presented a bar graph indicating that \$10,000 could be used to save either 9,900 dehydrated children, hundreds of pneumonia and tuberculosis patients, or one AIDS. Barton Gellman, *supra* note 186.

<sup>195</sup>*Id.*

patented in any sub-Saharan African nation (save for South Africa), meaning that these nations could, had they money, purchase Zerit at cost from generic manufacturers without violating patent law. For these countries, the problem was one of funding. In South Africa, however, the problem was also one of patents. Because BMS had not lowered its prices, South Africa desired to use compulsory licenses to either manufacture the drug themselves (as Brazil was doing) or purchase the drug from generic manufacturers. Thus in 1997, South Africa proposed a change in its laws that would have allowed for the compulsory licensing of essential medications. Such a policy is not inconsistent with TRIPS, the WTO provisions pertaining to international patent protections, but it nevertheless posed a threat to BMS' profits. Perhaps more than any other industry, the pharmaceutical relies on patents for profits. Thus BMS and the entire U.S. pharmaceutical industry, with the backing of the U.S. government, filed suit in South Africa to enjoin the proposed change in the law.<sup>196</sup> The intense lawsuit, which was finally dropped by the pharmaceutical industry in 2001, delayed South Africa's attempts to obtain Zerit at cost.

By 1998, pharmaceutical companies were waking up to the need to address the AIDS epidemic, if only to protect the goodwill of their brand. In August 1998, Sapirstein conceived of a plan to sell HIV/AIDS drugs, including Zerit, to the developing world at discounted prices. Poor countries and multinational corporations (whose employees in foreign countries were being infected by the thousands) would receive discounts ranging from 10% to 60%.<sup>197</sup> Perhaps due to the concern over parallel imports, BMS scrapped this plan and instead pursued a charitable program focused primarily on education, prevention and medical research. On May 6, 1999 BMS announced the launch of "Secure the Future," a program to which they committed \$100 million over 5 years.<sup>198</sup> Within two years, \$44.2 million had already been committed, including a \$19.6 million

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<sup>196</sup>Although the move by South Africa was legal under TRIPS, the United States viewed it as a significant threat to the nation's pharmaceutical industry. The New York Times Magazine reported that the Clinton administration "declared war" on South Africa and lobbied Nelson Mandela and Thabo Mbeki hard on the issue. Tina Rosenberg, *supra* note 144, at 52.

<sup>197</sup>Bill Brubaker, *supra* note 185.

<sup>198</sup>Bill Brubaker, *supra* note 185. Critics note that the actual cost of the program is much lower than \$100 million. First, it is tax-deductible. Second, roughly \$33 million of the \$100 million total is coming from funds already budgeted for charity that

clinical trial in Botswana led by the Harvard AIDS Institute.<sup>199</sup> This clinical trial is one of the few pieces of Secure the Future that will actually get medications into the hands of HIV/AIDS patients.

Although Secure the Future was a public-relations victory for BMS, the pharmaceutical industry continued to receive bad press for its high prices. On December 6, 1999, U.N. Secretary General Kofi Annan called for new “public-private partnerships” to help address the AIDS epidemic. The pharmaceutical industry responded to the call. So long as their patent rights would not be violated, the industry agreed in May 2000 to the “ACCESS” initiative to lower drug prices. Under the ACCESS initiative, prices of AIDS medications would be cut in poor countries by 90%.<sup>200</sup> Curiously, internal company projections called for increases in drug production to cover thousands of new patients in Africa, not millions.<sup>201</sup> As the production estimates indicate, ACCESS did not have quite the impact that one might have expected. Eight months after the program was announced, only one of the five companies, Glaxo Wellcome, was willing to even disclose its AIDS medicine discounts.<sup>202</sup> Prices, in general, remained well above cost – in December 2000 Zerit cost \$5 per day in South Africa and \$6.2 per day in Uganda. This was roughly half of its cost in the United States, but still well above the rate of 60 cents per day that Brazil obtained by manufacturing generics in state-owned labs.<sup>203</sup> (Brazil, like India but unlike South Africa, does not abide by patents.)

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will now be devoted to Secure the Future. And, third, the company can reduce the actual cost by valuing donated Bristol-Myers drugs at the wholesale prices it charges hospitals, rather than at the company’s much lower manufacturing costs. “Basically, Bristol-Myers Squibb is investing \$100 million to ensure that criticism from important sources is silenced,” said Nathan Geffen, a spokesman for Treatment Action Campaign, a South African AIDS activist group.

<sup>199</sup>Bill Brubaker, *supra* note 185.

<sup>200</sup>Barton Gellman, *A Turning Point That Left Millions Behind; Drug Discounts Benefit Few While Protecting Pharmaceutical Companies’ Profits*, WASHINGTON POST, Dec. 28, 2000, at A1.

<sup>201</sup>Barton Gellman, *supra* note 186.

<sup>202</sup>Barton Gellman, *supra* note 200.

<sup>203</sup>CARMEN PÉREZ-CASAS, MEDECINS SANS FRONTIERES, CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES, HIV/AIDS MEDICINES PRICING REPORT, SETTING OBJECTIVES: IS THERE A POLITICAL WILL? (Dec. 2000).

By 2001, millions of Africans had died of AIDS and millions more were infected. Neither Secure the Future nor the ACCESS initiative had succeeded in dropping the price of Zerit in sub-Saharan Africa, and particularly in South Africa. The situation was becoming untenable. Early in the year, Cipla, a generic drug manufacturer located in India, offered to sell to African nations a three-drug cocktail that included Zerit for \$350 per patient per year.<sup>204</sup> Meanwhile, a flurry of headlines tarnished the reputation of the pharmaceutical industry. The slogans of the activists – “Pfizer’s Greed Kills,” “Death Under Patent,” “Medical Apartheid” – went straight to the heart of the industry’s long-standing efforts “to portray itself as being driven by improving the human condition,” said Michael Artinger of Decision Resources, a pharmaceutical research firm.<sup>205</sup>

In March 2001, James Love, head of the Consumer Project on Technology, an advocacy group founded by Ralph Nader, pushed for the creation of a nonprofit company that could be granted a license to make and sell a low-cost version of stavudine.<sup>206</sup> His proposal relied on the fact that d4T had been developed with taxpayer funds, and he proposed to ask the government to exercise, for the first time ever, its march-in rights under Bayh-Dole to license d4T to his new nonprofit. Meanwhile, student activists at Yale University also seized upon the fact that d4T was not entirely a BMS product. After all, Yale itself held the patent.<sup>207</sup> BMS had at times argued that it could not lower prices because of its agreement with Yale, which held the patent and benefited from royalty payments.<sup>208</sup> Thus student activists called on Yale to grant additional

<sup>204</sup>Raquel Pontes de Campos, *supra* note 72.

<sup>205</sup>Barton Gellman, *supra* note 200. In addition, the pharmaceutical industry has also received negative press due to a perception that prescription drug prices are too high. In 2000, for the first time since 1995, shareholders brought resolutions asking drug companies to “create and implement a policy of price restraint on pharmaceutical products for individual consumers and institutional purchasers.” The proposal also asked for a report to shareholders on what efforts had been made to make products available “at reasonable cost.” The shareholder vote at BMS, sponsored by the Sinsinawa Dominicans, Sisters of St. Francis/Assissi, and Catholic Healthcare West, obtained 5% of the shareholder vote. INVESTOR RESPONSIBILITY RESEARCH CENTER, SOCIAL POLICY SHAREHOLDER RESOLUTIONS IN 2000: ISSUES, VOTES AND VIEWS OF INSTITUTIONAL INVESTORS (Jan. 2001).

<sup>206</sup>Raquel Pontes de Campos, *supra* note 72.

<sup>207</sup>Donald G. McNeil Jr., *Yale Pressed to Help Cut Drug Costs in Africa*, N.Y. TIMES, Mar. 12, 2001, at A3.

<sup>208</sup>Karen DeYoung & Bill Brubaker, *Another Firm Cuts HIV Drug Prices; Sub-Saharan Africa Is the Focus of Bristol-Myers*

licenses to manufacture and distribute d4T in Africa (in breach of Yale's contract with BMS). Yale refused to breach its contract but ultimately reached an agreement with BMS to "remove any obstacles" on patent and pricing issues. Yale spokesman Tom Conway stated that "as far as Yale is concerned, anybody who wants to give [Zerit] away, all the time, it's fine with us."<sup>209</sup> Interestingly, the efforts by James Love and the students at Yale were the first to incorporate into their activism the leverage created by the fact that both taxpayers and Yale contributed to the drug's development and retained certain rights to the medication.

*On March 14, BMS finally yielded to the mounting pressure and announced that Zerit would be made available in Africa for 15 cents per day. Together with Videx (or ddI), the cost would be \$1 per day.<sup>210</sup> The company calculated that this move would raise its total charitable commitment to Secure the Future from \$100 million to \$115 million. "This is not about profits and patents; it's about poverty and a devastating disease," said John L. McGoldrick, executive vice president, Bristol-Myers Squibb. "We seek no profits on AIDS drugs in Africa, and we will not let our patents be an obstacle."<sup>211</sup> After this announcement, the price of Zerit in South Africa slowly began to drop. At the time of this writing, one year later, there is evidence that Zerit is now available in South Africa roughly at cost.*

Of course, BMS and Yale were not the only parties with rights to Zerit – the U.S. government also retained rights to the medication. It is thus worth looking at the U.S. response to the AIDS epidemic in poorer nations.

While poorer nations demanded that the international framework soften patent rights when necessary to

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*Move*, WASHINGTON POST, Mar. 15, 2001, at A1.

<sup>209</sup>*Id.*

<sup>210</sup>The NIH licensed ddI (Videx) to BMS on the condition that the drug be made available at a fair price, but this clause "has never been enforced." Tina Rosenberg, *supra* note 144, at 52.

<sup>211</sup>Melody Petersen & Donald G. McNeil, Jr., *Maker Yielding Patent in Africa For AIDS Drug*, N.Y. TIMES, Mar. 15, 2001, at A1. *See also* Melody Petersen, *Abbott to Sell Low-Cost AIDS Drugs in Africa*, N.Y. TIMES, Mar. 28, 2001, at C9; and Melody Petersen, *Lifting the Curtain on the Real Costs of Making AIDS Drugs*, N.Y. TIMES, Apr. 24, 2001, at C1.



respond to health crises, richer nations, including the U.S., resisted these efforts. In April 2000, Brazil brought forward a nonbinding resolution to the U.N. Human Rights Commission asking that international agreements be “supportive of public-health policies” that promote affordable drugs and medical technologies. On April 23, 52 countries on the 53-member commission approved the proposal. The U.S. abstained. Then, in May, a WHO proposal to make drugs available at low prices failed under pressure from the United States. The U.S. recharacterized the health issue as a trade issue, arguing that the WTO, and not the WHO, should handle the issue.<sup>212</sup>

Meanwhile, at the WTO, the U.S. lobbied aggressively for a strong international patent regime. Exceptions in times of health crises were resisted. That is, they were resisted until the U.S., when faced with an anthrax scare at home, threatened to violate Bayer’s patent on Cipro. The hypocrisy of its position was untenable, and at the Doha round of WTO negotiations, poorer nations won a mild concession. Specifically, the Doha Declaration on the TRIPS agreement authorizes nations to manufacture generics for their own population when necessary to alleviate a major health crisis.<sup>213</sup> The effect of this provision is likely to be minimal, as few poor nations have the capacity to manufacture their own generics.

Meanwhile, throughout the epidemic the government declined to act upon its rights to the AIDS medications developed in part with government funding. On September 3, 1999, James Love and Ralph Nader sent a letter to Dr. Harold Varmus, Director of the NIH, asking the NIH to exercise its rights in government-funded inventions by granting a license to manufacture these medications to the WHO.<sup>214</sup> Specifically, they noted that the U.S. government possesses an:

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<sup>212</sup>Raquel Pontes de Campos, *supra* note 72.

<sup>213</sup>WORLD TRADE ORGANIZATION, MINISTERIAL CONFERENCE, FOURTH SESSION, DOHA, DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH (Nov. 14, 2001). *See also* Robert Weissman, *A Long Strange TRIPS: The Pharmaceutical Industry Drive to Harmonize Global Intellectual Property Rules, and the Remaining WTO Legal Alternatives Available to Third World Countries*, U. Pa. J. Int’l Econ. L. 1069 (Winter 1996).

<sup>214</sup>Letter from Ralph Nader, James Love, & Robert Weissman to Dr. Harold Varmus, Director of NIH (Sept. 3, 1999) (asking for NIH to give the World Health Organization, WHO, access to US government funded medical inventions) (the full text of the letter is available at <<http://www.cptech.org>>).

irrevocable, royalty-free right of the Government of the United States to practice and have practiced the invention on behalf of the United States and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement with the United States. 37CFR404.7(a)(2)(i)

Varmus declined to do so. In his response to the proposal, Varmus wrote that “in principle, the U.S. government can license patent rights to the WHO. . . . [But,] I do not believe that the lack of such a license from the NIH is inhibiting developing countries from addressing their needs. As you stated, many of these countries can issue compulsory licenses, and those that have not enacted that authority to date can do so if they choose. . . . The role of NIH in these sovereign matters is, appropriately, extremely limited.”<sup>215</sup> Two aspects of Varmus’ response are startling. First, Varmus’ response indicates that the executive branch was, in the handling of Zerit, simply not on the same page. Varmus argued that given South Africa’s capacity to pass compulsory licensing legislation, granting a license to the WHO was unnecessary. Meanwhile, however, other members of the Clinton administration were actively trying to block such legislation from coming into force. Second, Varmus’ desire to limit the role of the NIH in these complicated “sovereign” affairs runs contrary to the express terms of Bayh-Dole, which grants to the funding agencies alone the authority to exercise march-in rights. Taxpayers retain rights to essential medicines like Zerit, and at times national security and global equity might call for their exercise. If the NIH is not making this calculation on behalf of taxpayers, then who is? This issue will be further explored in the following section, along with numerous other issues pertaining to tech transfer that have been raised by the narrative account of Zerit’s development.

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<sup>215</sup>Letter from Dr. Harold Varmus, Director of NIH, to Ralph Nader, James Love & Robert Weissman (Oct. 19, 1999) (responding to their request calling on the NIH to provide the World Health Organization (WHO), access to government-funded medical inventions) (the full text of this letter is available at <<http://www.cptech.org>>).

## IV.

### **Zerit’s Implications for the Direction of Technology Transfer Policy**

This section of the article uses the narrative of Zerit to inform current debates over the direction of technology transfer. Generally speaking, Zerit indicates that technology transfer policy is working well. A health crisis emerged, and the government responded. Throughout the 1980s, government funding for AIDS prevention, education and medical research increased dramatically (though, admittedly, not fast enough for some). Scientists at NIH labs in Bethesda performed critical foundational research. Scientists at universities, funded both by the government and by private industry, focused their attention on compounds with potential activity against the AIDS retrovirus. When a promising compound was discovered, Bristol-Myers negotiated an exclusive license and committed to seeing the drug through the clinical trials process. To help speed this process along, the government chipped in funds, approved Zerit for “investigational use,” and expedited the FDA approval process. Just five years after the clinical trials began, Zerit was on the market. Zerit’s development largely corroborates the conventional wisdom regarding Bayh-Dole’s success.

At the same time, Zerit also reveals that some tinkering may be in order. Adjustments to the policy are possible to make because tech transfer, like the R&D that it regulates, is in a near constant state flux. Of course, Zerit is only one example of how technology transfer is operating in practice; one must take care not to extrapolate too much from this single narrative. Nevertheless, it can be used to shed light on the three current questions pertaining to tech transfer that were presented in Section II. The narrative also reveals that a few questions should be added to the list.

#### **IV.A. The Three Current Questions Revisited**

*IV.A.1. Are Exclusive Licenses Necessary to Ensure Commercialization of Government-Funded Inventions?*

Zerit seems to indicate that exclusive licenses are indeed necessary to ensure commercialization. The cost to BMS of developing Zerit is estimated to be in the neighborhood of \$150 million to \$300 million.<sup>216</sup> This is less than the average cost of developing a new drug, mostly due to increased government support for the development of AIDS medications. It is nevertheless a large chunk of change. No company would undertake such an expenditure without the security of knowing that they would enjoy, for some period of time, market exclusivity in rich nations.

Perhaps in the 1940s and 1950s, when the clinical testing and approval processes mandated by the FDA were less stringent, nonexclusive licenses were enough to do the trick. Zerit, however, indicates that by the late 1980s this was no longer the case. The only way d4T might have reached the market, absent an exclusive license, would have been for the government to take the drug all the way through the clinical trials and approval process itself, and then to license it to a generic manufacturer for distribution. Among medications, an AIDS medication would have been a strong candidate for this. First, there was significant pressure on the U.S. government to expend resources developing AIDS drugs. Particularly in the early 1990s, when Zerit was undergoing clinical trials, pressure on the government to devote more resources to AIDS was considerable. Second, because of the high level of awareness within the AIDS community of the drugs in the pipeline, Zerit needed very little in the way of advertising and promotion. These activities are typically thought better done by private entities than by public, but, here, perhaps the government could have handled it. Nevertheless, the government chose not to follow this path, and it does not appear likely

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<sup>216</sup>See discussion *supra* page 75.

the government will do so in the near future. Assuming it does not, exclusive licenses may be necessary to ensure commercialization.

#### *IV.A.2. Are Taxpayers Maximizing the Return on Their Investment?*

Zerit indicates that taxpayers are getting a significant return on their investment, but that they are not maximizing their return. Access to Zerit is a significant taxpayer return, and it is enjoyed by virtually all U.S. citizens (save for the small number falling in the cracks between Medicaid and ADAP). Tax revenues obtained from sales on Zerit are another significant return. However, the profit that BMS has earned on Zerit far exceeds that necessary to have ensured commercialization. A high estimate of the cost to BMS of Zerit's development is \$300 million. By the end of 2000, BMS' revenues on sales of Zerit exceeded \$2.3 billion. The patent continues to run until 2008. Needless to say, this is a remarkable return on investment. It is fair to say that had BMS known *a priori* that its revenues would have been only \$1 billion, it still would have been in the company's interest to spend \$300 million on the drug's development. It follows that BMS has benefited and continues to benefit from a sizeable windfall. (The story of Zerit reveals, perhaps, why in the 1990s biotech industry profits exceeded those of all other industries.)<sup>217</sup> Some of this corporate windfall might be funneled back into R&D on other medications. Some might be returned to shareholders. But why should the company's managers and shareholders be the ones deciding how this windfall will be spent? Shouldn't this money have remained in the hands of consumers?

One comprehensive way to reign in this corporate windfall would be for Congress to pass the Sanders

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<sup>217</sup>Barton Gellman, *supra* note 200.

amendment.<sup>218</sup> An easier path, and one that would not require congressional action on new legislation but rather implementation of existing legislation, would simply be the exercise of (or even the credible threat of exercising) march-in rights. March-in rights were, after all, designed to prevent exactly the corporate windfall that BMS is currently enjoying. It can reasonably be argued that BMS has not achieved “practical application” in the marketplace because they are not making Zerit available on “reasonable terms.” Exercise of march-in rights would not, in this instance, require establishing a formula for what constitutes a reasonable price. Rather, one need merely find that revenues exceeding \$2.3 billion on a government-funded drug that cost private industry roughly \$300 million to develop is a *prima facie* case of unreasonability.

There are two reasons to believe why the occasional, judicious use of march-in rights will not chill industry’s willingness to commercialize government-funded inventions. First, when Bristol-Myers originally negotiated its exclusive license for Zerit in 1988, the Bayh-Dole regime was only eight years old. At that time, there was still reason to believe that the march-in rights had teeth, yet, Bristol-Myers went ahead with the drug’s development anyway. Second, the government simply plays too big a role in foundational R&D for private industry to completely walk away from the table. So long as a calculation of “reasonable terms” allows for a reasonable profit – a profit high enough to entice commercialization – then government-funded inventions will not be left to languish in government and university labs.

It is also worth noting that the lack of a reasonable pricing mechanism like that contained in the march-in provisions may be creating a *disincentive* for private industry to spend capital on R&D. Under the current regime, greater private investment in the development of a government-funded drug is not rewarded with greater property rights (such as a longer patent term). Thus BMS had no incentive to contribute more to

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<sup>218</sup>A discussion of this amendment is provided, *supra* note 107.

Zerit's development. Indeed industry has every incentive to sit back and wait for the government to push the R&D along. This is especially true in the case of essential medicines (such as Zerit) where the company knows that the government is under pressure to speed drugs through the clinical testing and FDA approval process. If instead pricing requirements were keyed to the extent of industry's role in the development process, then industry would have a greater incentive to expand their role in collaborative research.

In addition to exercising march-in rights, the government should also act to maximize the taxpayer return on investment by implementing and enforcing more stringent disclosure requirements. The proposal put forth by the NIH is a positive step in this direction.<sup>219</sup> The proposal put forth by TACD would be even better.<sup>220</sup> There is reason to believe that were BMS forced to disclose its actual expenditures on Zerit, maintaining the company's goodwill would require maintaining a reasonable pricing strategy.

#### *IV.A.3. Is Technology Transfer Facilitating Research in a Way That Maximizes Human Health?*

Zerit serves as a reminder that scientific progress often depends on openness. When neither Dr. Prusoff nor Bristol-Myers possessed the technical capacity to test d4T for activity against the AIDS retrovirus, they turned first to the NIH and then to Emory University for assistance. In 1986, Dr. Prusoff never imagined that he might someday earn millions of dollars from sales of d4T. Today, this possibility is not only recognized by scientists, but it often drives their research. Under these circumstances, would Dr. Prusoff have been so willing to collaborate with Dr. Schinazi at Emory?

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<sup>219</sup>NIH RESPONSE, *supra* note 5, at 14.

<sup>220</sup>TRANS ATLANTIC CONSUMER DIALOGUE, *supra* note 121.

If, as some critics suggest, university scientists are becoming increasingly reluctant to exchange information, then medications like Zerit may take longer to develop. Thus the warnings of these critics should be investigated and taken very seriously. Two areas of information exchange in particular warrant attention. First, more attention should be given to “material transfer agreements” (MTAs), the agreements that regulate the process by which researchers share information. There is some evidence that research is being impeded by the fact that corporations and universities each have their own, complicated MTAs.<sup>221</sup> The government should push for greater uniformity in the field, and should also push for maximum openness in MTAs involving federally-funded inventions.

Second, greater consideration should be given to university conflicts of interest policies. It was very important to Dr. Prusoff that Bristol-Myers’ initial grant of \$500,000 to Yale University (given in exchange for a right of first refusal) came with no strings attached. The university scientists maintained complete academic freedom. Academic freedom must be preserved and, more importantly, the potential for personal profit must not be allowed to interfere with the purposes of academic research.

#### **IV.B. Adding Two More Questions to the List**

The narrative of Zerit further reveals that two more questions should be added to the current debates over the future of tech transfer.

##### *IV.B.1. What are the International Implications of Tech Transfer?*

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<sup>221</sup>Paulette Walker Campbell, *Pacts Between Universities and Companies Worry Federal Officials; Research agencies fear that the restrictions in some agreements may impede scientific progress*, CHRONICLE OF HIGHER EDUCATION, May 15, 1998, at A37.



Technology transfer is an international issue. It is a national security issue. It is a health issue. And it is an ethical issue. It is not, as the United States argued before the WHO, only an issue of international trade. U.S. citizens are paying to support biomedical R&D and, based on their investment, they retain certain rights to their invention. The decision on when and exactly how to exercise these rights should be made by government officials who consider all of the relevant issues. Taxpayers deserve no less.

Zerit indicates that no arm of the executive branch is conducting this calculus on behalf of U.S. citizens. Dr. Varmus, Director of the NIH, declined to help alleviate the AIDS epidemic in Africa by licensing stavudine to either the WHO or a nonprofit organization (that would have sold the drug to African nations at cost). Varmus acknowledged that, under Bayh-Dole, the government retains the right to do so. Nevertheless, Varmus decided that the role of the NIH in these “sovereign matters” is “extremely limited.”<sup>222</sup> Considering that Bayh-Dole expressly asks the directors of funding agencies (like the NIH) to oversee the exercise of the government’s retained rights, Varmus’ position amounts to an abdication of executive authority. Under the terms of Bayh-Dole, the role of the NIH is anything but “limited” – indeed the NIH is *the* agency endowed with this power. The NIH must assert, in accordance with the express language of Bayh-Dole, the power to exercise march-in rights on behalf of U.S. citizens. If not, action must be taken to bestow this power elsewhere in the administration.

It is also worth noting that while the NIH abdicated its Bayh-Dole responsibilities, no other arm of the executive branch stepped in to fill the gap. Indeed Zerit reveals that different arms of the executive branch were in fact working at cross-purposes. Varmus argued that because African nations could have pursued compulsory licenses on their own, additional licensing was unnecessary. Meanwhile, the Department of

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<sup>222</sup>Letter from Dr. Harold Varmus, *supra* note 215.

Commerce and the highest levels of the Clinton administration lobbied to prevent South Africa from passing just such a scheme.

Finally, Zerit reveals that when the NIH does, in the future, take a hard look at whether to exercise march-in rights, it must take care not to confuse the issue of patents from the issue of parallel importation. The administration's opposition to South Africa's scheme of compulsory licensing is a patent issue – compulsory licenses, though valid under TRIPS, pose a threat to the profits derived from patents. The issue of pricing – the issue at the heart of the government's case to exercise march-in rights – is *not* a patent issue. Rather, it is an issue of parallel importation. All across sub-Saharan Africa, BMS priced Zerit at well over cost. The BMS pricing strategy was driven by the fear that the drug would find its way back into the U.S., thus undermining the company's critical base of sales. There is some reason to doubt this fear. After all, Brazil and India have both been producing large quantities of stavudine, and there is little evidence that these pills have found their way back into the U.S. Nevertheless, the issue of parallel importation is an important one.<sup>223</sup> As Zerit indicates, it is certain to play a role in any situation where a poor country needs access to a drug that is being sold elsewhere at a high price. When the next such situation arises, the government would do well to distinguish this issue from the issue of patents.

#### *IV.B.2. Should Different Drugs Receive Identical Treatment Under Tech Transfer?*

Zerit indicates that tech transfer could be made more effective by distinguishing drugs developed in response to major epidemics from other drugs. Such a policy has two justifications. First, drugs developed in response to major epidemics are likely to be the subject of more challenging ethical and humanitarian pressures.

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<sup>223</sup>For information on the current debate over parallel importation, see, e.g., Editorial, *Importing Cheaper Drugs*, N.Y. TIMES, Sept. 29, 2000; <<http://www.wipo.int>>; <<http://www.cptech.org>>.

Second, these drugs are likely to be the product of greater than average public support. Communities affected by the AIDS epidemic placed extraordinary pressure on the U.S. government to act. Within just a few years, government support for foundational AIDS research jumped by several hundred million dollars.<sup>224</sup> And the government's support did not stop there. By 1990, taxpayers had contributed \$428 million to the AIDS Clinical Trials Group.<sup>225</sup> And, due to the extent of the epidemic, the government also contributed in other ways: The FDA granted Zerit "parallel track" status, enabling for relatively inexpensive clinical testing on over 13,000 patients; and, the FDA expedited the approval of Zerit, an essential medicine, by requiring that Phase III testing achieve only a surrogate, and not a final, endpoint.

Because essential medications like Zerit are both the subject of heightened ethical considerations and the product of greater-than-average government support, these medicines should be subject to greater government-retained rights. There are strong reasons why march-in rights should be exercised in the case of Zerit, and the same might be expected of other essential medicines. However, exercising these rights might instill fear in industry, the fear that the government will begin to exercise these rights in lots of other medications. Distinguishing essential medicines from other medicines will strengthen tech transfer by enabling the government to exercise their rights in the former without threatening private industry's investment in the latter.

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<sup>224</sup>*AIDS in the Third World*, *supra* note 138.

<sup>225</sup>Philip Hilts, *Panel Issues Broad Attack on U.S. Response to AIDS*, N.Y. TIMES, Aug. 22, 1990, at B4.

## V.

### Conclusion

Twenty years have passed since the Bayh-Dole Act fundamentally altered the government's approach to technology transfer. This legislation encouraged the use of exclusive licenses to stimulate private investment in the commercialization of government-funded inventions. It is widely recognized that the Act has succeeded in achieving this goal. Scientists operating with federal funds are increasingly attuned to the commercial applications of their work. The number of FDA-approved medications has skyrocketed, and there are now hundreds of small biotech firms pushing potential medications through the product pipeline.

The development of Zerit confirms that the Bayh-Dole Act is a success. Nevertheless, Zerit also indicates that some tinkering may be in order. Such tinkering is possible to enact, for technology transfer policy, like the R&D that it regulates, is the subject of near-constant tinkering. Specifically, Zerit indicates that taxpayers are not maximizing the return on their investment, for, under current policy, private industry is able to earn profits in excess of those that are necessary to induce commercialization. In the case of Zerit, Bristol-Myers Squibb turned a \$300 million investment in a taxpayer-funded medication into more than \$2.3 billion in revenue, and this in the midst of a staggering AIDS epidemic.

To the current debates over the direction of tech transfer policy, the story of Zerit adds two important considerations. First, when citizens pay for biomedical R&D, they retain rights to the subject invention. The government has a responsibility to act upon these rights in accord with public health, national security, international trade and ethical and moral responsibility. Bayh-Dole entrusts the NIH with the power to make

this calculation, but, in the case of Zeret, the NIH abdicated its critical role. Either the NIH must assume its obligation to make this difficult calculation, or, this responsibility should be delegated to another arm of the executive branch. Second, it might be possible and indeed preferable for tech transfer to distinguish essential medicines from other medicines. The former are likely to be the product of increased government support and the target of increased demand for access. Distinguishing them from other medications would enable the government to act upon their retained rights to these essential medications without upsetting the balance of rights at play in other medications.